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TRANSCUTANEOUS NERVE STIMULATION AND CHRONIC PAIN



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"Truth is rarely pure and never simple"
(Oscar Wilde)



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This thesis is based upon the following publications, which in the text will be referred to by their Roman numerals:

- I Eriksson, M.B.E., Sjölund, B.H. and Nielzén, S.: LONG TERM RESULTS OF PERIPHERAL CONDITIONING STIMULATION AS AN ANALGESIC MEASURE IN CHRONIC PAIN.
Pain, 6, 335-347, 1979.
- II Eriksson, M.B.E., Sjölund B. and Sundbärg, G.: PAIN RELIEF FROM PERIPHERAL CONDITIONING STIMULATION IN PATIENTS WITH CHRONIC FACIAL PAIN.
Manuscript.
- III Sjölund, B.H. and Eriksson, M.B.E.: THE INFLUENCE OF NALOXONE ON ANALGESIA PRODUCED BY PERIPHERAL CONDITIONING STIMULATION.
Brain Res., 173, 295-301, 1979.
- IV Eriksson, M.B.E., Rosén, I. and Sjölund, B.H.: THERMAL SENSITIVITY IN MAN IS DECREASED BY A CENTRAL MECHANISM AFTER TRANSCUTANEOUS NERVE STIMULATION.
Manuscript.
- V Nielzén, S., Sjölund, B.H. and Eriksson, M.B.E.: PSYCHIATRIC FACTORS INFLUENCING THE TREATMENT OF PAIN WITH PERIPHERAL CONDITIONING STIMULATION.
Pain, 13, 365-371, 1982.
- VI Borgenstam, C., Eriksson, M.B.E. and Hagberg, B.: PERSONALITY FACTORS AS PREDICTORS OF ADJUSTMENT TO CHRONIC LOW BACK PAIN.
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INTRODUCTION

General considerations

The word pain may be applied to a wide range of subjective experiences from the perception of an experimental stimulus such as brief electrical shocks to the agonizing, persistent pain in certain types of terminal cancer. In a biological frame of reference, pain alerts the individual on threatening or actual tissue damage. It is a protective mechanism which is indispensable for normal life, as documented by the fate of those rare individuals with congenital absence of pain sensitivity (Jewesbury 1970).

In medical practice, pain has been and still is the most common symptom. Carl von Linné, in 1763, listed pain as one of his clinical classes of diseases. Chronic pain may be caused by long-standing pathological processes in somatic or visceral structures, by prolonged dysfunction of parts of the nervous system and, in contrast to acute pain, it can also be caused by psychopathological mechanisms (see Sternbach 1974). In 1979, it was estimated that over 700 million work-days a year were lost in the United States, due to chronic pain (Bonica 1980). In Sweden, with a population of approximately 8 millions, the sale of analgesics in 1981 was SEK 150 millions (Svensk Läkemedelsstatistik 1982).

There is a difference between the sensory aspect of a painful stimulus and the relating emotional experience. Pain is a personal event which derives its importance from predictions of the future and means of control. A basic element in this event is anxiety, closely coupled to factors such as meaning and expectancy. In some human subjects, the aversive effect of painful stimuli was reduced by the mere belief that they could be terminated (Bowers 1968, cf. Egbert et al. 1964). The significance of the pain message is a major factor in determining the suffering therefrom (Beecher 1956). Women in childbirth, soldiers wounded in battle and Buddhist monks walking on fire, under certain circumstances may not at all experience pain (cf Merskey & Spear 1967, Melzack 1973).

Classifications of pain

On qualitative grounds, the sense of pain has, Procrusteanly, been put into two major categories:

- a) bright, distinct and well-localized, superficial pain
- b) dull, aching and ill-localized deep pain.

Superficial pain is normally described as cutaneous whereas deep pain may be related not only to visceral structures but also to somatic structures beneath the skin, such as muscles, ligaments, bones and joints (Lewis 1942, cf. Cervero 1980). If superficial pain is produced by a needle piercing the skin, an easily localized sensation is felt, so called first or initial pain. This is followed, within a second, of a dull, burning sensation which is more difficult to localize, so called second or delayed pain (Lewis 1942, Schmidt 1981). Superficial pain, notably initial, is a powerful arousing stimulus, as seen e.g. in the EEG, and usually gives rise to withdrawal reflexes and a general sympathetic response with increased motor activity. Deep pain is often characterized by other autonomic responses such as nausea, sweating and lowered blood pressure and frequently inhibits motor activity (Wolff & Wolf 1958). Pain which requires medical attention may be looked upon as acute or chronic. Acute pain initiates diagnostic measures and, if possible, etiological treatment. When no cause is found or there is no etiological treatment available but the pain continues relentlessly, symptomatic treatment is what remains.

Psychological aspects of pain

Every pain condition is coloured by the personality and cultural background of the individual and by emotional reactions to the physical illness (see Merskey & Spear 1967). It is an interesting observation that some physiological characteristics of acute pain, such as increased cardiac rate and muscle tension, are similar to those of anxiety, whereas the characteristics of many patients with chronic pain also may be seen in depression, e.g. disturbances of sleep and appetite, irritability and social withdrawal (Sternbach 1974). Pain may also be due to psychological or emotional causes and arise e.g. as a conversion disorder, as an unconscious means

of eliminating anxiety from concern with the stresses of life (Engel 1951, cf. Pilowsky 1969). Sometimes pain may even involve an element of interpersonal communication, such as the 'painmanship', originally described by Szasz in 1968 (cf. Berne 1964).

Symptomatic pain relief

It is usually possible to relieve acute pain by pharmacological agents or blocking of the appropriate nerve or nerves with local anesthetics. In addition, these methods can be helpful in the relief of chronic pain of limited duration, such as cancer pain. They have proven less useful in long-standing chronic pain of benign origin (see Houde 1980, Merskey et al. 1980). Until the last decade the only alternative when the conventional approaches to chronic pain had failed, was a neurosurgical intervention. The interruption of anatomical structures recognized as 'pain pathways' usually gives temporary relief but many times pain reappears, sometimes more intense and more resistant to therapy. Dorsal rhizotomy, cordotomy and thalamotomy are still used, mainly in certain types of terminal cancer pain (White & Sweet 1969). However, pain perception is a complex phenomenon and the mechanisms by which neurosurgical procedures relieve pain are not completely understood.

Neurobiology of nociception, pain and analgesia

Definitions

The terms pain and nociception are here used in accordance with the recommendations by the International Association for the Study of Pain, (Merskey et al. 1979, Table 1).

Table 1. Definitions according to the International Association for the Study of Pain.

NOXIOUS	A noxious stimulus is a tissue damaging stimulus.
NOCICEPTOR	A receptor preferentially sensitive to a noxious or potentially noxious stimulus.
NOCICEPTION	Activity induced in the nociceptor and nociceptive pathways by a noxious stimulus.
PAIN	An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.

Evoking activity in nociceptive afferents by experimental methods has, of course, neurophysiological phenomena in common with acute pain. Analogies between the two have yielded important knowledge, particularly concerning mechanisms for superficial pain. Recently, animal models for chronic pain have come into use, which bear more similarities to human chronic pain situations. The ethical questions involved in experimental work on nociception and pain were reviewed recently (Iggo 1979, Sternbach 1979).

Pathways transmitting nociceptive information

Nociceptors, located in most organs, are normally excited by potentially harmful mechanical, thermal or chemical stimuli. The afferent fibers from the nociceptors are found among the thin myelinated A-delta fibres with a conduction velocity of about 5-30 m/s (Adriaensen et al. 1981) and unmyelinated C-fibers with a conduc-

tion velocity of about 0.5-1 m/s (Torebjörk 1974). The difference in conduction velocity is thought to be related to the separation in time between first and second pain (see Torebjörk & Hallin 1979, cf. Zotterman 1939). Most central processes of thin fibres reach the spinal cord via the dorsal roots. They project one or two segments rostrally and caudally and terminate mainly in the outer layers of the dorsal horn. Neurons in lamina II and III, the substantia gelatinosa, appear to have a relation both to incoming afferent terminals and to dendrites of neurons in the deeper laminae (Cervero & Iggo 1980). In the dorsal horn there are synaptic connections to motor and sympathetic reflex chains as well as to ascending pathways. One problem of interpretation is that there appears to be a marked convergence of peripheral afferents of different modalities to many central transmission cells (see Willis and Coggeshall 1978).

Among the spinal projection neurons, few of which seem to mediate nociceptive information exclusively, those in the contralateral anterolateral quadrant appear to be particularly important for the perception of pain in man. As the ascending tracts traverse the brain stem there are synaptic connections with the reticular formation at several levels. Many fibres terminate in the medial reticular nuclei of the medulla such as the nucleus raphe magnus. More rostrally, some fibres give collaterals, to the mid-brain reticular formation and the periaqueductal gray area. The nociceptive information reaches the thalamus via the spinothalamic tract and possibly via more indirect routes. Thus, in several species, medially passing fibres, some relayed through the brain stem, are reported to terminate in the medial and intralaminar nuclear complex, whereas laterally passing, more direct fibres terminate in the posterior nuclear complex (see Willis & Coggeshall 1978, Yaksh & Hammond 1982). From the latter region fibres, probably including those transmitting nociception, project on to sensory areas of the cerebral cortex (see Basbaum 1980). In addition, some fibres from medial thalamic nuclei may ascend to the cerebral cortex to terminate more diffusely (Roos et al. 1982). However, pain is rarely an ictal aura phenomenon in epilepsy or produced upon

electrical stimulation of the cortex (White & Sweet 1969). Some aspects of the nociceptive information is probably transmitted also to the hypothalamus and other parts of the limbic system (see Nathan 1977, Yaksh & Hammond 1982).

When activity, evoked by nociceptive stimuli, is recorded in higher parts of the central nervous system, the interpretation is hampered by the simultaneous activation of arousal mechanisms by such stimuli (cf. Starzl et al. 1951). Moreover, the relation between neuronal activity and perceptual phenomena is complex (Libet 1973).

Possible mechanisms of chronic pain

The nociceptors may be sensitized to natural stimuli by changes in their microenvironment (Beck et al. 1974, see Torebjörk & Hallin 1979), such as the local release of small amounts of algescic substances (see Zimmermann 1979).

Transient neural activity can be elicited in normal coarse and thin sensory axons by rapidly applied direct pressure. Minor compression of the spinal ganglion, however, produces long periods of repetitive firing. Under pathological conditions, the functional properties of the neurons may be considerably altered, e.g. resulting in markedly increased mechanosensitivity with sustained firing upon acute compression of an axon (Howe et al. 1977). Mechanisms of this kind may explain pain in chronic sciatica and nerve compression syndromes. When Wall and Gutnick (1974) transected the sciatic nerve in rats and prevented regeneration, end neuromas formed. These showed unusual properties, being continuously active in the absence of any intentional stimulus. The spontaneous firing was believed to originate in myelinated small diameter afferent fibres. Such changes might cause pain following traumatic nerve lesions, amputations or surgical procedures.

Chronic pain may also originate in the central nervous system, as demonstrated e.g. by a report of phantom pain in the lower extremities, occurring in patients with surgically verified, complete

spinal transection (Melzack & Loeser 1978). Spontaneous activity from deafferented neurons was suggested as a possible cause. When deafferentation is incomplete, neurons undergo changes which may lead to the formation of new aberrant connections (see Guth 1974, Tsukahara et al. 1975). The sensitivity of the synaptic membrane e.g. to naturally released transmitter might also increase (cf. Zimmermann 1979). Interestingly, deafferentation pain is said to be reproducible in some patients, by electrical stimulation of the related somatosensory cortex (see Tasker et al. 1980). Dysfunction of the inhibitory control systems, which will be discussed in the following section, is yet another possible mechanism in pain after lesions in the central nervous system.

Inhibitory control systems

The nervous system is not a passive recipient of sensory input as illustrated e.g. by discriminatory phenomena, such as focusing of attention. Afferent signals are selected, modulated, integrated and channelled to a multiplicity of structures including the neurons controlling effector organs, ultimately governing the individual's behaviour.

Early observations indicated that the total pattern of cutaneous sensory input was an important factor in determining the quality of the sensation (see Lewis 1942). The negative dorsal root potential (DRP), evoked by stimulation of large myelinated fibres, received attention by Barron and Matthews, (1938). It was later interpreted as reflecting presynaptic inhibition of primary afferent fibres by depolarisation (Eccles et al. 1962). In 1964, Mendell and Wall reported that stimulation of unmyelinated fibres elicited a positive DRP, which they interpreted as presynaptic hyperpolarization, i.e. presynaptic facilitation. They also found stimulation of large fibres to elicit a brief response from central transmission cells, whereas activation of thin fibres gave a prolonged discharge (Mendell & Wall 1965). This and other experimental, as well as clinical evidence, in 1965 led Melzack and Wall to formulate "the gate control theory" for pain. It proposed that activity in large

fibres, by presynaptic inhibition closed a 'gate' to small fibre activity and, moreover, had a negative feedback action upon the large fibres themselves. Conversely, activity in thin fibres would open the 'gate' for onward transmission by presynaptic facilitation. The segmental interaction was supposed to be mediated by substantia gelatinosa neurons. A suprasegmental control mechanism was also included in the theory.

It is now well established that the activity elicited in certain dorsal horn neurons by nociceptive stimulation can be inhibited by simultaneous activation of low threshold cutaneous receptors in or close to the receptive field of the neurons (Brown et al. 1973, Handwerker et al. 1975). The topographically organized segmental inhibition seems to be at least partly postsynaptic and, on the whole, shows a rather close relation to the duration of the stimulus. The positive DRP found by Mendell and Wall and interpreted as presynaptic facilitation has, however, not been confirmed (Jänig & Zimmermann 1971, see also Schmidt 1972). In fact, Mendell later found the positive DRP to be a secondary phenomenon caused by decreased afferent depolarisation but only reproducibly in terminals belonging to coarse muscle afferents (Mendell 1972). Also on clinical grounds, arguments against the gate theory have been put forward. There is for example no relation between the complaint of pain and the nerve fibre spectrum in pathological conditions affecting peripheral nerves (Dyck et al. 1976, see also Nathan 1976).

Recently, however, in recordings from single C-fibre afferents, hair deflections presumably mediated via large fibres caused a lowering of the antidromic excitation threshold of the C-fibre terminals whereas pinching, mediated via thin fibres, caused an increase of threshold, implying presynaptic inhibition by large fibres and facilitation by thin fibres (Hentall & Fields 1979). This would support the original hypothesis of Melzack and Wall (1965).

Since Sherrington and Sowton in 1915 reported on the increased flexor reflex after spinal transection, suprasegmental control of spinal transmission has become well established. Thus, Hagbarth and Kerr (1954) studied the synaptic effectiveness within the cat spinal cord and observed that afferent spinal conduction through the dorsal and contralateral ventral columns was modified by electrical stimulation of bulbar and mid-brain reticular structures and of the sensori-motor cortex.

A detailed analysis of inhibitory and excitatory descending control on spinal cord neurons was subsequently carried out by Lundberg and his colleagues. They found several different descending systems, exerting mainly postsynaptic inhibitory effects on interneuronal transmission in spinal reflex arcs. Mechanisms producing primary afferent depolarization were also found to be influenced (see review by Lundberg 1982). Descending systems seem to influence also the size and properties of peripheral receptive fields, e.g. via connections on interneurons (Hillman & Wall 1969, see Willis and Coggeshall 1978).

Renewed interest in the descending control of spinal transmission and its relation to nociception and analgesia arose from the demonstration of anti-nociceptive effects by weak electrical stimulation of medial brain stem areas (Reynolds 1969). Effective sites were found notably in the mesencephalic periaqueductal gray matter (Mayer et al. 1971, Liebeskind et al. 1973, Mayer & Liebeskind 1974). Oliveras, Besson and others, by intracellular recordings from dorsal horn neurons, showed that electrical stimulation of caudal brain stem nuclei, particularly the nucleus raphe magnus, had selective inhibitory effects on activity evoked in these cells by noxious stimulation (see Fields & Basbaum 1978). In man, long-lasting inhibition of chronic pain has been reported upon electrical stimulation in the periaqueductal gray matter of the brain stem as well as in posterior thalamic regions (Hosobuchi et al. 1977, Boivie & Meyerson 1982). A powerful inhibition of

convergent noxious and non-noxious input to some dorsal horn neurons could, in addition, be produced by another noxious stimulus applied to wide-spread areas of the animal's body surface. This effect has been named the diffuse noxious inhibitory control (DNIC) and is most likely produced by the descending systems just described (LeBars et al. 1979a, 1979b). A close correlation has been shown between the intensity of the noxious stimulation and the degree of diffuse inhibition.

The pain experience and behaviour may ultimately be influenced by activity in the frontal lobes, believed to exert a control on human affective behaviour. They are suggested to have a role also in functions such as anticipation, by presetting neural mechanisms in response to predicted incoming stimuli and by modulating shifts of attention or activity in response to changes in the environment. Frontal lobe lesions have been shown to result e.g. in affective disturbances, such as a dissociation of emotions from sensory experience or excessive responses to affective stimuli. The latter is known also from certain thalamic lesions and might then be due to removal of frontal control (see Warren & Akert 1964).

Pharmacological aspects

Opiates, i.e. morphine and morphine-like compounds, are acknowledged as a group of drugs which most efficiently alleviate many types of acute and chronic pain. However, in man, even large doses of narcotic analgesics do not reliably relieve experimental pain (see Beecher 1959).

A rapid expansion of opiate research started with the discovery of specific opiate receptors in the vertebrate central nervous system (Pert & Snyder 1973, Simon et al. 1973, Terenius 1973). In monkeys and humans, limbic structures including the hypothalamus, caudal brain stem areas, i.e. the nuclei raphe magnus and gigantocellularis, as well as the dorsal part of the spinal cord gray matter were found to have a high opiate receptor density, whereas the

density of most cortical areas was low (Kuhar et al. 1973, LaMotte et al. 1978). Further studies have demonstrated several receptor types (Lord et al. 1977, cf Martin 1967). Endogeneous brain ligands were soon discovered (Hughes et al. 1975, Terenius & Wahlström 1975) and now constitute three classes of opioid peptides (see Höllt 1983). The smallest are the pentapeptides, leucine- and methionine-enkephalin. The endogeneous opioids are collectively known as the endorphins and seem to be widely distributed within the central nervous system. In several species, dense enkephalin-like immunoreactivity is seen e.g. in the brain stem and in superficial layers of the dorsal horn (see Hökfelt et al. 1980).

The widespread distribution both of receptors and of endorphinlike immuno-reactivity suggests that opioids influence many processes in the central nervous system. Early studies on the action of opiates were based mainly on systemic administration, lesions and micro-injections. Microinjection of morphine into medial brain stem structures was known to produce antinociceptive behavioural effects (Tsou & Jang 1964, Herz et al. 1970). Later, a more complete mapping showed the effective area in primates (Pert & Yaksh 1974) to extend from the rostral portions of the fourth ventricle along the cerebral aqueduct into regions surrounding the caudal portions of the third ventricle. There is a partial correspondence between effective sites for opiate microinjection and those producing analgesia on weak electrical stimulation as well as with the distribution of opiate receptors and enkephalin-like immunoreactivity (see Basbaum 1982).

A specific spinal effect of the opiates was soon demonstrated (Yaksh & Rudy 1976, Duggan et al. 1976, see also Yaksh 1981), as would be expected from the distribution of opiate receptors and enkephalin-like immunoreactivity. Presynaptic as well as postsynaptic sites of action have been suggested (see Zieglgänsberger 1982). The spinal action of opiates has been therapeutically utilized for postoperative analgesia as well as for severe pain in terminal cancer (Wang et al. 1979, cf. also Eriksson et al. 1982).

Another technique to study the functional role of endorphins is to employ the specific opiate antagonist naloxone (Jasinsky et al. 1967). The blocking of antinociceptive effects by this substance has been taken to suggest a role of endogenous opiates in this respect. Such observations include the analgesia by weak electrical stimulation in the brain stem in animals (Akil et al. 1976) or man (Adams 1976, Hosobuchi et al. 1977) and the increases in experimental pain thresholds found after needle acupuncture in man (Mayer et al. 1977). However, other analgesic effects such as those induced by intravaginal manipulation in the female rat (Komisaruk & Wallman 1977) and hypnosis in man (Goldstein & Hilgard 1975) are reported not to be naloxone reversible.

The fact that naloxone does not always block the analgesia from antinociceptive procedures may reflect both that naloxone does not effectively block all subtypes of receptors (Lord et al. 1977) and that other, non-opioid, systems are involved in producing the analgesia. Thus, analgesia produced by stimulation in the brain stem is abolished when a descending serotonergic dorsolateral funicular pathway is pharmacologically manipulated (Besson 1980) or cut (Basbaum et al. 1977). Some results indicate that antinociceptive effects produced by morphine microinjections in the brain stem are mediated via descending, both catecholaminergic and serotonergic pathways, (Yaksh 1979).

Thus, analgesic mechanisms appear to involve multiple descending systems which can be activated by different routes and probably contain different transmitters. Even more complex is the picture after the discovery that one neuron may contain both a classical transmitter and one or several peptides in addition (Hökfelt et al. 1980). It has not been established whether the peptides are transmitters in the true sense or rather modulate the release of a classical transmitter or its postsynaptic effects (see Zieglgänsberger 1982).

Pain relief by afferent stimulation

Historical aspects and general considerations

If the potent segmental and suprasegmental control systems, now known to exist, have a physiological role in the perception of pain, one might expect the activity level of the systems to be influenced by environmental stimuli, nociceptive in particular. Indeed, the pain relieving effect of counterstimulation, notably painful, has been acknowledged for long. Cupping is a method known from primitive medicine as is application of mildly painful heat, e.g. the burning of moxa fibres in association with acupuncture, a slightly painful stimulus by itself. The ancient technique of 'electro-analgesia' was originally performed with electrical fish, most likely a painful procedure (see Kane & Taub 1975) and, more recently, painful electrical stimulation with brief pulse trains at 3 or 10 Hz, was shown to alleviate chronic pain for several hours (Melzack 1975a). The pain-relieving effects of painful counter-stimulation, as well as of acupuncture, might well be related to inhibitory control mechanisms of the DNIC type (vide supra), which are triggered by noxious input from many parts of the body.

There are also every day observations on the pain relieving effects of increased non-noxious sensory input. Rubbing and massaging as a cure for pain are techniques probably known since the dawn of time. Vibration, heat and cold are also long known modalities for pain relief (Gammon & Starr 1941, Melzack et al. 1980, Ottosson et al. 1981) just as therapeutic electrostimulation, which was widely used in the western world less than a century ago (Beard & Rockwell 1881). It declined in importance with the appearance of oral analgesics and anaesthetic techniques as well as neurosurgical approaches to the relief of chronic pain. Renewed interest arose, however, from the formulation of the 'gate control theory' and the underlying experimental evidence predicting that stimulation of large diameter peripheral nerve fibres would raise the threshold for detecting injury, in the region served by the stimulated nerve.

Stimulation trials related to the 'gate control theory'

Wall and Sweet in 1967, in eight patients with chronic pain, demonstrated that peripheral non-painful sensory stimulation, applied for few minutes, would abolish intense pain for up to 30 minutes. The current intensity and spread had to be adjusted so that a 'tingling' sensation appeared in the painful region, for the analgesic effect to appear. The results were appreciated as a clinical confirmation of the gate control hypothesis, although the duration of pain relief was not anticipated by the theory. Later criticism was based partly on this and other contradictory evidence from clinical experience with electro-stimulation (Nathan 1976).

Other attempts at relieving pain by activating the spinal 'gate' were made with low intensity electrical stimulation of the dorsal columns (Shealy et al. 1967) and this technique (dorsal column stimulation, DCS) was soon found to be effective in relieving chronic pain in man (Shealy et al. 1970). The physiological basis for pain relief from DCS, however, is uncertain, since analgesia has been reported also with the electrodes applied to the ventral surface of the cord (Larson et al. 1975). The unpredictable early results in combination with the risk of complications urged the development of an instrument for patient selection. Peripheral nerve stimulation via surface electrodes or so called transcutaneous nerve stimulation, here denoted conventional TNS, was then tried since the types of afferents stimulated were thought to be the same for the two techniques. It soon turned out, however, that conventional TNS in itself gave promising results, and being a non-invasive technique it came into widespread use within a relatively short time.

Conventional transcutaneous nerve stimulation

Conventional TNS as introduced by Wall and Sweet (1967) employed stimulation of peripheral nerves with a frequency of approx. 100 Hz and an intensity which produced paresthesiae in the painful area. Surface, needle or implanted electrodes were used. From their initial results it was evident that TNS could give poststimulatory pain relief for a period of time which considerably exceeded the period of stimulation. Portable stimulators soon became commercially available and a number of clinical trials were published on the use of conventional TNS to relieve chronic pain (Table 2). Surface electrodes were routinely used and intermittent stimulation prescribed.

Table 2. Immediate and long-term pain relief with conventional TNS

Year	Author	No of patients	Immediate results	2-6 months follow-up	12 months follow-up
1974	Shealy	759	40 %		
1975	Cauthen and Renner	113	50 %	32 %	
1975	Ebersold et al.	230	58 %	33 %	
1975	Loeser et al.	198	68 %		12.5 %
1975	Picaza et al.	100	55 %		
1975	Ray	396(?)		64 %	20 % (?)
1976	Long	197	67 %		38 %

In the studies reported in Table 2 there are marked variations in immediate success rates, 40-68 %, which might be due to differences in patient selection, in protocol and instruction as well as in the criteria of success used. Patients with chronic 'low back pain' dominated the reports. Shealy (1974) reported that 310/759 chronic pain patients had excellent or good pain relief from conventional TNS. More than 50 % of the patients were 'lumbar disc failures'. Also intercostal neuralgias, postherpetic neuralgias, phantom limb pain, causalgia, thalamic pain syndromes and other pain conditions were treated. A few reports on long-term effects (Table 2) revealed that the success rates decreased markedly as the observation time increased. A considerable variation was still seen, 12.5-38 %, after 12 months observation time. In spite of differences in design between the studies, it was evident that the majority of chronic pain patients were not helped by conventional TNS in the form used. A number of factors might have been responsible for the unsatisfactory results, apart from those already mentioned. One obvious such factor would be variations in the technical effectiveness of the equipment, i.e. did sufficient activation of relevant excitable structures occur?

Technical aspects. If presynaptic inhibition is an important element in TNS (Melzack & Wall 1965), a necessary prerequisite for a satisfactory result would be to stimulate coarse cutaneous afferents, known from animal studies to induce presynaptic inhibition in terminals belonging to all cutaneous afferents (see Schmidt 1971). Thus, the technical aspects of TNS are worthy of a close consideration.

When a voltage is applied between two points on an exposed bundle of nerve fibres or on a bundle buried in tissue, a current will flow between the points. Since large diameter axons have a low inner longitudinal resistance, more current will pass through these fibres than through thin fibres. Hence, with a suitable adjustment of the voltage applied, fibre activation can be limited to the coarse fibres (see Koester 1981). When surface electrodes are

used, the configuration of the electrodes, their position in relation to the nerve fibres stimulated and characteristics of the tissue structure will influence the resulting current density at the axonal membrane. This is the important parameter in determining the absolute amount of charge necessary to activate these axons (Burton & Maurer 1974, McNeal 1976). For example, the current necessary for single fibre activation in intracortical microstimulation with sharp pointed electrodes is $<5 \text{ uA}$ (Stoney et al. 1968).

The first generation of TNS stimulators showed a wide diversity of stimulus wave forms and either had no compensatory system for the impedance in the patient circuit at all or were based on the constant voltage principle (Long & Hagfors 1975). When laboratory stimulators producing constant current were tried, they were found more effective in relieving pain than the devices delivering constant voltage (Shealy & Maurer 1974, Picaza et al. 1975). Electrode size in relation to skin irritation was also looked at and a minimum surface area of 4 cm^2 recommended in order to minimize the risk (Shealy & Maurer 1974). Since the impedance in the electrode - patient - electrode circuit with this electrode size will vary in the 2000-3000 Ohm range (unpublished observations) the stimulator should provide constant conditions with an external load in at least this range to be efficient.

A number of sinusoidal, spike, ramp and rectangular wave forms as well as combinations thereof, were tried initially. No convincing evidence was found that any one was superior to a simple monophasic rectangular pulse as regards patient comfort and pain relief (e.g. Ray and Maurer 1975). Another important aspect in the stimulation of nerves is illustrated by the classical strength/duration curves, which relate the pulse width and current intensity necessary for threshold excitation. Studies on the excitability of exposed cat saphenous nerve showed that for excitation of C-fibres, a pulse width of about 75 times that of A-beta fibres was needed.

A-delta fibres were excited by a pulse width about 20 times that of A-beta fibres. In all application of conventional TNS, the pulse width used is far below that needed for C-fibre activation. On the other hand, it is well above the pulse width needed for A-alfa and A-beta activation and suffices, at higher intensities, also for activation of A-delta fibres (see Li & Bak 1976). The effective pulse width for conventional TNS treatment, judged by patient preference, was in one study found to be within the 50-150 usec range for 16 of 19 patients with good or excellent pain relief (Linzer & Long 1976). The effective frequencies were between 20 and 60 Hz for 14 of the 19 patients.

Effective electrode sites for pain relief with conventional TNS were usually found to be over the painful region or over the nerves to the involved area (e.g. Loeser et al. 1975). Several reports pointed out that the electrode location was a critical factor and stressed that several locations often had to be tried. Satisfactory pain relief was found to be associated with a feeling of 'tingling' within the area of pain (Linzer & Long 1976, cf. Wall & Sweet 1967). In a few studies, however, pain relief was reported from subliminal stimulation as well as from stimulation of remote or contralateral sites (Picaza et al. 1975, Laitinen 1976).

Electroacupuncture

Sharp objects or needles inserted and mechanically manipulated at well defined points on the body surface, so called acupuncture, was used several thousand years ago in China to treat disease and pain, localized e.g. in joints, low back, epigastrium or abdomen (Essentials of Chinese Acupuncture 1980). The ideas eventually reached Europe and, in several countries, became widely used (e.g. Manaka 1972). The French practitioner Sarlandière (1825) was interested in the pain relieving effects of the technique. He began to use the needles as electrodes, connected to charged Leyden bottles, which might be considered as the first attempt to perform electroacupuncture. In China, the cultural revolution in 1966 meant a reevaluation of the partly disreputed

traditional Chinese medicine. Electroacupuncture was introduced and became widely recommended for analgesia during surgery. It is still used and reported to give a fairly reliable and reproducible hypalgesia for some types of surgery, notably on the neck and head (Kaada et al. 1974). Needles are then placed in acupuncture-points or in the auricles and most commonly stimulated electrically at a low frequency (0.5-5 Hz). The stimulation is adjusted so that visible muscle twitches occur or to a level just tolerated. A local 'tehchi' feeling, meaning slight soreness, numbness or a sense of swelling, is considered desirable (Essentials of Chinese Acupuncture 1980, cf. Chang 1978). For chronic pain, electroacupuncture is more rarely used in China (own observation) than in the West (e.g. Stux et al. 1981, Sodipo 1979).

Electroacupuncture was shown to elevate experimental pain thresholds by Eastern (Research Group of Acupuncture Anaesthesia, 1973) as well as Western research groups. Andersson et al. (1973, 1977) found an increase of the electrical threshold for tooth pulp pain, which appeared gradually, with a latency of 15-30 minutes. It was seen only when the current intensity produced forceful muscle contractions at a low frequency (1-5 Hz). The threshold increase slowly returned to baseline values during another 30 minutes. Chapman and co-workers (1976, 1977) replicated the study, confirming that intrasegmental stimulation was more efficient than extrasegmental in elevating the threshold for dental pain. The strong muscle contractions reported necessary, suggested that activation of deep afferents was important. This supported the observations of Chiang and co-workers (1973), who showed that a selective cutaneous block (n. radialis superficialis) of a stimulated acupuncture point did not abolish the corresponding pain threshold elevation, whereas it completely disappeared following a procain block of the nerve branches supplying the deep tissues underlying the point (n. ulnaris and medianus).

Acupuncture-like transcutaneous nerve stimulation

The increases in pain threshold recorded during low frequency electroacupuncture were seen also when the needles were replaced by surface electrodes (Andersson et al. 1973). However, this technique did not efficiently relieve chronic pain when tested in a small group of patients. In contrast to healthy subjects, patients with chronic pain did not tolerate the high intensity needed to produce strong muscle contractions with single pulses and good pain relief was reported only in one of 12 patients studied (Andersson et al. 1976). Interestingly, non-painful stimulation with such low frequencies has so far not been reported to produce pain relief.

However, in spite of the results of Andersson and co-workers, the pain threshold increase after electroacupuncture with needle or surface electrodes seemed worthy to explore further. A necessary prerequisite for the use of surface electrodes seemed to be a technique to evoke forceful muscle contractions in a manner tolerable to patients with chronic pain in a nearby area. It would also be valuable if the technique could be administered by the patient himself.

Technical aspects. To achieve these goals, a technique was devised where the single pulses in electroacupuncture were replaced by short (70 msec) pulse trains. The trains were delivered at a low repetition rate (1-2 Hz), with the intention to allow forceful muscle contractions to build up and resolve (Eriksson and Sjölund 1976). In fact, the internal frequency of the trains employed (100 Hz) exceeds the fusion frequency of most mammalian skeletal muscles (Cooper and Eccles 1930). Subsequent clinical experience showed that most patients in chronic pain felt comfortable when muscle contractions in this way were elicited via surface electrodes, applied over mixed nerves or small muscle branches segmentally related to the area of pain. Since this low frequency technique had several aspects in common with certain forms of acupuncture,

it was denoted acupuncture-like TNS. Conventional and acupuncture-like TNS will, in the following text, be collectively referred to as TNS.

In addition, it was considered necessary to standardize the electrical stimuli given, by employing the constant current principle in a design overcoming an external load of about 2500 Ohm (cf. supra). Finally, a suitable pulse shape and duration had to be selected and since no convincing evidence could be found against a monophasic square wave pulse, this was chosen at a duration of 200 usec. To facilitate the clinical routine, a stimulator was designed according to the above mentioned specifications, which could produce either type of pulse pattern, conventional or acupuncture-like TNS.

In a first clinical trial, 50 consecutive patients with long-standing chronic pain were instructed to use TNS intermittently. All patients used conventional TNS during the first week, and if this technique failed to relieve their pain, acupuncture-like TNS for the second week. After an observation period of one month, 20/50 patients reported satisfactory relief with conventional TNS. Ten of the remaining 30 patients were relieved of their pain by changing to acupuncture-like TNS (Eriksson & Sjölund 1976). It thus seemed as if this modification of the electroacupuncture technique was a valuable addition for the alleviation of chronic pain by TNS.

AIM OF THE PRESENT STUDY

Against the background given an attempt was made to answer the following questions:

1. What are the long-term results from the use of transcutaneous nerve stimulation (TNS), administered in a technically adequate manner?
2. What benefit is added by the use of acupuncture-like TNS?
3. Is the etiology and characteristics of pain related to the outcome of TNS treatment?
4. What mechanisms are responsible for the analgesia from acupuncture-like and conventional TNS? In particular, do opioid systems contribute to the analgesia produced?

It became gradually apparent in the clinical work that psychiatric factors and personality traits influenced the outcome of symptomatic TNS therapy as well as the social rehabilitation of the patient. An attempt was therefore made also to answer two questions related to these problems.

5. Can patients who fail to be relieved of their chronic pain by TNS treatment be identified through a psychiatric evaluation?
6. What personality factors are of importance for a successful social adjustment in chronic pain patients reporting satisfactory pain relief from symptomatic treatment, e.g. with TNS?

MATERIAL AND METHODS

Patients

The patients in these studies were all referred for symptomatic pain treatment to a tertiary level interdisciplinary pain unit, at the University Hospital in Lund. Most had chronic pain of many years duration, none less than six months. Examinations and treatments were usually given on an out-patient basis. The patients were referred to the pain unit by consultants after a thorough screening including neurophysiological, neuroradiological and other diagnostic procedures in a search for conditions where etiological treatment would be possible. Most patients had tried several types of symptomatic pain treatment previously, including pharmacological agents and surgical procedures. Since TNS stimulators have been shown to interfere with heart synchronous pacemakers (Eriksson et al. 1978), no patient with a pacemaker was allowed to participate.

Methods

The quantitative assessment of pain

Pain is an emotional as well as a sensory experience and categories or values chosen to describe pain cannot be looked upon as 'false' or 'true', but rather as more or less helpful parameters in the intended respect. In chronic pain there is usually no detectable stimulus and there may not be any observable physical signs and therefore no immediate indications of the severity of pain.

In the present studies, we chose to measure pain by the non-traumatic, easily administered, visual analogue scale according to Clarke and Spear (1964), (cf. Pilowsky & Kaufman 1965). This graphic representation of pain is a 10 cm long printed line with the end-points defined as 'no pain' and 'excruciating pain', meaning pain as bad as it could be. After careful instruction in

the use of the scale, the patients were asked to mark the point which represented the level of pain at the time of observation. They were each time given a new scale and did not have access to earlier ratings. The visual analogue scale has the advantage of being relatively independent of language or verbal capacity (cf. Melzack 1975 b) and avoids some of the difficulties involved in categorical scales, e.g. deciding what categories should be used (Huskisson 1974). However, it did present problems to a small number of patients little used to or with difficulties of abstract thinking. Although the marking on the visual analogue scale, as with any other type of test or scale, is open to influences from the observer, it has proven sensitive to changes in the level of chronic pain and reliable over time (Joyce et al. 1975).

Variations in the level of pain over longer periods of time have also been assessed by information obtained through a standardized set of questions administered to the patients at regular intervals. Changes in analgesic drug consumption were noted as were changes in physical functioning, such as the estimated time spent reclining, sitting or walking and participating in social activities (cf. Ray 1975, Sternbach 1975, Chapman et al. 1981).

Transcutaneous nerve stimulation (TNS)

By conventional TNS is meant electrical stimulation of large diameter cutaneous afferents via surface electrodes at a frequency of 30-100 Hz. The current intensity is approximately 1.5-2.5 times the sensory threshold and paresthesiae or 'tingling' sensations in the area of pain are usually reported.

By acupuncture-like TNS is meant electrical stimulation of mixed nerves or efferent motor fibres via surface electrodes. Short pulse trains with an internal frequency of 100 Hz are given at a low repetition rate, 0.5-3 Hz. The current intensity is approximately 2.5-5 times the sensory threshold and visible muscle contractions are usually evident.

The protocol used for evaluating the pain-relieving effect of TNS was in all studies the same. The patients were initially instructed in the use of conventional stimulation. Only if this failed to produce significant pain relief, was acupuncture-like stimulation tried. There were practical reasons for this, since a limited number of stimulators producing acupuncture-like TNS were initially available. Acupuncture-like stimulation producing strong muscle contractions, might also cause physical difficulties to perform other activities simultaneously and is more obvious to the environment. All pain medication was discontinued at least six hours prior to the first TNS session. Before beginning the stimulation, each patient's pain was evaluated and its extent mapped. The patients in study I were told that TNS might or might not affect the pain. The patients with facial pain were told not to expect to be able to control ongoing attacks and warned that stimulation might actually worsen such an attack.

Stimulation was first attempted over nerves innervating the painful area. Secondly, stimulation within or enclosing the area of pain was tried. For acupuncture-like TNS an attempt was first made at activating muscles, innervated from the spinal segment related to the distribution of pain. Secondly, muscles within the painful area were considered. As a last alternative for both methods, applications over trigger points (Melzack et al. 1977) or modifications based on suggestions from the patient, were used.

In all patients the sensory threshold was noted, i.e. the amplitude at which the stimulation pulses were just perceived as a weak tingling sensation, provided there was a good electrode-skin contact. The actual stimulation strength then used for therapeutic purposes was chosen in relation to threshold value. The stimulation frequency for conventional TNS varied between 100 Hz, the maximum of the stimulator used, and 30 Hz. For acupuncture-like TNS, 2 Hz was chosen as the initial repetition rate with individualized slight adjustments between 0.5 and 3 Hz. The intrinsic frequency of the pulse train was constant at 100 Hz. The patients were instructed

to try different frequencies and use what was most comfortable, while giving good analgesia. The current intensity for conventional TNS was usually 1.5-2.5 times the sensory threshold, an intensity which generally produced a strong tingling sensation, but not pain. This relates well to the relative strength necessary to excite most A-beta-fibres but not A-delta-fibres of a composite nerve bundle (cf. Trouche & Massion 1980). At a pulse train duration of 70 msec, used in acupuncture-like TNS, stimulus intensities of 2.5-5 times the sensory threshold were not painful, and in most patients produced visible muscle contractions. The duration of the stimulation period initially recommended was 30 minutes, repeated three times daily. Later, this was varied according to individual differences in the duration of the analgesia as well as in pain intensity and frequency.

Naloxone as a tool to study opioid systems

Naloxone is considered a fairly pure opiate antagonist when used in low doses (Jasinsky et al. 1967). As different subtypes of opioid receptors in the central nervous system successively were discovered, it became apparent that the affinity of naloxone was not equal to all types. It now seems that naloxone most effectively blocks the mu-receptor whereas for example leucine-enkephalin appears to have its greatest affinity for the delta-receptor (Lord et al. 1977).

All patients in our series were given at least two injections of 1.6 mg naloxone each, before the response was considered definitely negative (III). When naloxone is used to reverse overdoses of narcotics affecting respiration, 0.4 mg is the usual initial dose. This may be repeated with 2-3 minutes intervals. If no effect is seen after 2-3 injections, the symptoms are considered not to be opiate-related. However, as much as 10 mg has been given to humans in an attempt to reverse placebo analgesia (Levine et al. 1978). Generally, results from studies using naloxone as an indicator to exclude involvement of opioid systems, must be interpreted with care (cf. Hill 1981).

Measurement of thermal sensory thresholds

Afferent neuronal systems mediating thermoception have a close anatomical relation to those mediating nociception (see Willis & Coggeshall 1978). We therefore used thermoception as a model for nociception (IV) and measured thermal sensitivity quantitatively by the Marstock technique, modified after Fruhstorfer and co-workers (1976). A thermostimulator operating according to the Peltier principle was applied to the thenar region. The ceramic contact area could be warmed or cooled at a rate of $1.0\text{--}1.5^{\circ}\text{C/sec}$, and the direction of the temperature change reversed via a hand-held switch button. In normal subjects, warm sensation was usually detected in the $34\text{--}38^{\circ}\text{C}$ range and cold sensation in the $31\text{--}34^{\circ}\text{C}$ range. The neutral temperature zone (the warm-cold difference limen) in the thenar region was usually $2\text{--}5^{\circ}\text{C}$. The skin surface temperature was monitored on a calibrated chart recorder. Environmental conditions were kept constant and the spontaneous skin temperature in the thenar region required to be $\geq 30^{\circ}\text{C}$ before each recording.

Psychiatric evaluation

Chronic pain patients in whom TNS treatment failed to relieve pain, were consecutively referred for a psychiatric evaluation (V). Among patients experiencing good or excellent pain relief from TNS, a control group was chosen, as far as possible matched for sex, age and duration of pain. The control patients were referred for the same psychiatric evaluation, arbitrarily intermingled with the TNS failures. We chose to refer all patients to the same psychiatrist although this meant a restriction on the size of the control group, since the psychiatrist could only assign a limited time for this task. The psychiatrist did not have access to the medical records and during the interview questions related to the outcome of TNS treatment were avoided. The evaluation was done with respect to five diagnostic categories:

1. Mental illness, meaning organic psychosyndromes including senile lesions and psychoses including endogenous depressive states with somatic manifestations, such as loss of appetite, early awakening and motor retardation.
2. Pathological personality traits, when the patients showed clear signs of at least one item such as evasion, denial, projection, severe rigidity or affective instability.
3. Situational problems, e.g. marked problems in personal relationships, economical matters or work situation.
4. Reactive mental decompensation, meaning neurasthenic, anxious or depressive reactions or evidence of accentuation of earlier neurotic symptoms in relation to the pain condition.
5. Normality, for patients who showed no positive evidence of any of the above four categories.

The diagnostic categories were chosen for their presumed usefulness in clinical routine work, having implications for what therapeutic approach might be of value for the individual patient. Thus, it was felt that patients in the first and fourth category might benefit from a continuous therapeutic contact with a psychiatrist. Patients in the third category were thought to benefit particularly from social and psychological support whereas for patients in the second category little could be offered from a therapeutical point of view.

Psychological assessment

Ten patients with chronic low back pain of long duration were selected according to a clinical evaluation with reference to social adjustment. A psychological assessment of the patients' so called 'adaptive capacity' was performed.

One way to perform psychological testing is by means of questionnaires. However, since this type of testing relies on the patient's own appreciation of himself in a particular situation, it seems to be an unreliable tool for the prediction of treatment outcome in

Table 3. Psychological tests used (VI)

Test and main function assessed	Discriminating power of the test	Reference
<u>Koh's_block_design</u> measures visuo-spatial ability	Correlates well with general intelligence; sensitive to brain damage.	Kohs, 1923
<u>Synonyms_Reasoning_Block</u> SRB:1 measures verbal ability	Correlates well with general intelligence.	Dureman and Sälde, 1959
SRB:2 measures logical-inductive ability	Correlates well with general intelligence.	Dureman and Sälde, 1959
<u>Colour_Word_Test,_CWI</u> measures how cognitive performance is affected by factors such as stress, anxiety and depression	Correlates well with psychiatric diagnoses e.g. depression. Distinguishes well between symptom neurosis and character neurosis.	Smith and Nyman, 1959
<u>Arrow-Dot_Test,_IES</u> measures the ego strength in relation to id and superego	Identifies subjects with impulsive and rigid behaviour.	Dombrose and Slobin, 1958
<u>Defence_Mechanism_Test,_DMT</u> assesses habitual defence mechanisms in dealing with anxiety	Differentiates well between neurotic and normal subjects. Predicts professional success e.g. in pilots and attack divers.	Kragh, 1959, 1961, 1962 cf. Neuman, 1978

chronic pain, as suggested by the considerable variation in results published (cf. Cummings et al. 1979, Pondaag & Oostdam 1979). We chose to evaluate cognitive ability and some personality aspects, thought to indicate the individual's ability to adapt to stressful situations, by using the tests in table 3. The factors expected to correlate with good social adjustment were above average intellectual level, a good ego-strength as measured by the Arrow-Dot test, stable response patterns to the stress situation presented by the Colour-Word test, and solid, mature defence mechanisms as revealed by the DMT-test. The latter is a particularly valuable addition over conventional personality inventory questionnaires, such as the commonly used MMPI (Dahlstrom et al. 1960). It has for example proven valuable in the selection of individuals suitable to be trained as airplane pilots by assessing what type of adjustment can be expected under severe stress conditions (Kragh 1961, cf. Neuman 1978).

RESULTS AND COMMENTS

TNS as a long-term therapy for chronic pain

- I: 123 patients with long-standing chronic pain of varying etiology and location, consecutively referred to the pain unit, were treated with TNS and followed for at least two years or till they terminated the treatment. If conventional TNS induced useful pain relief, it was continued. If it did not, instructions for acupuncture-like TNS were given and if this method was successful in alleviating pain, it was continued. If none of the two TNS-techniques gave useful pain relief, the patient was registered as a failure. On repeated occasions, the pain intensity was scored on a visual analogue scale before and after TNS. Records were kept of stimulation parameters, the duration of poststimulatory pain relief and how often the stimulator was used. Changes in analgesic medication and the patient's social and physical activity was noted with irregular intervals.
- II: Apart from the need for alternative therapeutic methods among patients with intractable facial pain (IFP), it seemed of great interest for the evaluation of the TNS technique to test and follow a group of patients with rather uniform chronic pain, as to type and location. In a prospective study, 50 patients with IFP of long duration, consecutively referred for consideration of neurosurgical treatment, were informed about the symptomatic nature of treatment with TNS. Consent was obtained to try this method before any surgical procedure was contemplated. There were 21 patients with typical "tic douloureux" and 29 patients with atypical IFP, 18 of whom had a traumatic, cerebrovascular or inflammatory etiology of their pain. The same TNS protocol was used as in study I and the patients followed for two years or till they terminated the treatment.

After one year, 10 of the 123 patients had died (I). They all had good/excellent pain relief from TNS until their death. Four patients were in spontaneous remission. Among the remaining 109 patients, 46 (42 %) had useful pain relief from TNS. After two years, three more had died and another two were in remission. Among the remaining 104 patients, 35 (34 %) still used TNS as their main analgesic. Among the 50 patients with chronic facial pain (II), after one year two had died and one was in spontaneous remission. Among the remaining patients, 24/47 or 51 % had satisfactory pain relief. After two years, when one more had died, and three were in spontaneous remission, 20/44 (45 %) of the remaining patients

Table 4. Long-term results with respect to etiology

Author, year	TNS-type	Etiology of chronic pain	n	Follow - up (months)				
				≤ 1	2-6	7-12	13-24	25-36
Gregg, 1978	conv. TNS	Posttraumatic facial pain	30		20 %			
Wynn Parry, 1980	"	Brachial plexus avulsion	98	30 %	20 %			
Bates & Nathan, 1980	"	-Low back; periph. nerve lesions; central pain -Postherpetic	161 74	48 % 35 %		27 % 20 %	16 % 15 %	
Sindou & Keravel, 1980	"	-Radicular syndromes -Periph. nerve lesions -Postherpetic neuralgia -Brachial plexus lesions -Central pain	28 55 34 28 22	60 % 87 % 67 % 25-30 % 0-11%				80 %
Bohm, 1978	Conv.+Acup. like TNS	Periph. nerve injury with sympathetic activity	24			42 %		
Eriksson et al. 1979	"	-Neuralgia, face -Neuralgia, other location -Rhizalgia -Central pain -Other organic etiology -Psychogenic pain	11 32 22 18 23 17		82 % 56 % 64 % 67 % 52 % 18 %	45 % 34 % 60 % 50 % 39 % 18 %	34 % *	
Eriksson et al. 1983	"	Facial pain	50		58 %	51 %		45 %

* See text, p. 39

were still using TNS as their main therapy for pain relief. Thus, in this study, only three failures were registered later than three months after TNS treatment started (Table 4).

When the pain relief from TNS was $> 50\%$, according to the visual analogue scale, social and physical activity was increased in half of the patients at the one year follow up and 44% of the patients had substantially reduced their analgesic intake (I). Among the patients reporting less than 50% decrease of their pain by TNS only a few were more active or had markedly lowered their intake of analgesic agents (I). In the group of patients with facial pain, seven who had been collecting sick benefits for a long time, went back to work (II).

For the patients in study I, the duration of poststimulatory pain relief was usually maximal during 1-3 hours after 30-60 minutes stimulation. This meant that TNS was usually applied 2-4 times daily. A few patients were seen with either no after-effect at all, having to use the stimulator continuously or with very long duration of the effect, which meant using TNS only 2-7 times a week. In 6/123 patients the after-effect became successively shorter, a phenomenon resembling tolerance (I). In some patients, pain relief was noted only after several days of stimulation (I, II, cf. Wynn Parry 1980). This 'cumulative' effect was particularly notable in typical trigeminal neuralgia. Several patients reported a successive decrease in the frequency and intensity of pain attacks only after 1-2 weeks of regular stimulation 3-4 times daily (cf. Gregg 1978).

The frequency preferred for conventional TNS was usually in the 60-100 Hz range, and for acupuncture-like TNS 1-2 Hz. Once a patient had settled for one or several sets of parameters, these were kept rather constant. Some patients used separate combinations of parameters for each of several particular pain feelings, appearing on different occasions.

Side-effects were few and local. Skin irritation and erythema was observed in approximately 10 % of the patients. In two, a serious allergic skin reaction was seen. However, in these patients treatment could continue with different electrodes and tapes. The stimulation was reported to intensify pain temporarily by 18 patients among the first 123 (I). Changes in stimulation frequency and intensity did not alter the situation (cf. Picaza et al. 1975). Nine of these patients, all eventually recorded as failures, had a positive psychiatric evaluation. Four patients with paroxysmal facial pain (II) reported worsening if TNS was used during the attacks but benefitted from stimulation when it was used between attacks. There was no suspicion of a major psychological cause of the pain in these patients. However, they were not subjected to a psychiatric evaluation.

Relation conventional TNS/acupuncture-like TNS

In the first group of 123 patients, acupuncture-like TNS added approximately 1/3 to the success rate at 3 and 12 months, and slightly less at 24 months (I). In the group of patients with facial pain (II) the usefulness of acupuncture-like TNS was even more evident. Whereas only 16 of 50 patients (32 %) experienced significant pain relief with conventional TNS, acupuncture-like stimulation relieved another 13 patients. In all, 29 of 50 patients (58 %) had satisfactory analgesia with TNS at the three months follow-up. In this group, the relation of acupuncture-like TNS to conventional TNS remained largely unchanged after one year and two years. A small number of patients, using mainly acupuncture-like TNS, turned to conventional TNS every now and then, and vice versa.

There were 54 patients with cutaneous hypesthesia/dysesthesia in and around the area of pain (I). Only nine were helped by conventional TNS after one year, whereas acupuncture-like TNS helped another 15 patients. In fact, all patients using acupuncture-like TNS at the one and two year observation time, had cutaneous hypesthesia. In the group with facial pain (II), no

significant difference in cutaneous sensibility was found between patients responding to conventional and acupuncture-like TNS. As regards the type of pain treated, conventional TNS seemed most effective when pain was localized to skeleton or joints (I). Acupuncture-like TNS was particularly useful in pain from muscle tissue (unpublished observations) and in radiating pain (I). There were 22 patients with rhizopathy. Only six were helped by conventional TNS at three months. Acupuncture-like stimulation successfully relieved pain in another eight patients, which gave a total number of 14, successfully treated (I).

Etiology and characteristics of pain in relation to the outcome of TNS treatment

Some of the first studies, using conventional TNS only, found criteria of importance for pain relief to be the pain characteristics and etiology. "Boring, throbbing, burning or cold" pain with evidence of a neurogenic lesion, i.e. pain which at least partly originated from an injury to the nervous system itself, was reported to be frequently relieved (e.g. Picaza et al. 1975). Conversely, TNS had little effect on pain of predominantly psychogenic origin (e.g. Long 1976). However, diagnostic criteria were missing in many reports and diagnostic grouping sometimes obscure.

When our results were analysed with regard to the existence or lack of a relevant organic etiology of the pain condition, significantly better results at the 3 months observation time were found among patients with a known organic etiology of the pain (I, II). Among the 17 patients with a positive psychiatric evaluation, only three patients experienced pain relief with TNS (I). Interestingly, seven of the eight patients with groin or perineal pain were found in this group. The eighth had a surgically treated rectal cancer and useful pain relief from conventional TNS. Among the 46 consecutive TNS failures analysed (V), 28 patients were diagnosed as having mental illness or pathological personality traits according to our classification (see Methods). Furthermore, there were

22 patients in this group, in whom the somatic investigations did not find a relevant organic cause of their pain.

The variations in underlying somatic etiology, as well as the location of pain, also influenced the results (Table 4). At three months, 9 of 11 patients (I) and 29 of 50 (58 %) patients (II) with facial neuralgia had good or excellent pain relief from TNS. Neuralgia in other locations (I), commonly of postherpetic, posttraumatic or postoperative origin, was relieved in 18 of 32 (56 %) patients. Cervical and lumbosacral rhizopathies (22 patients) were successfully treated in 64 %. The composite results from all patients with peripheral neurogenic lesions (I), showed a success rate of 63 % (41/65), at three months follow-up.

Pain from lesions in the central nervous system was significantly relieved in 12 of 18 patients. Of these, 5 of 7 patients with a lesion rostral to the spinal cord were considerably helped by TNS. Eleven of the patients had damage to the spinal cord and roots. Pain at the level of the lesion responded well to TNS (6/7), whereas pain distal to the lesion seemed unresponsive (1/4). Dorsalgia, lumbar or thoracic, was considerably relieved in all but one of the 7 patients. Patients with pain due to cancer growth were only rarely referred to the pain unit. In the few patients treated, pain caused by cancer metastases to the skeleton seemed more responsive to TNS (4/6 patients) than pain due to cancer growth in visceral structures (1/5 patients) (I). Later, unpublished observations confirm that visceral pain rarely is relieved by any of the TNS methods.

The influence of the pain characteristics and duration on TNS results were also examined (II). Continuous dull pain appeared more responsive than paroxysmal pain. There was also a significantly higher success rate among patients with a pain history of less than six years as compared to those with a longer history (II). Thus, a considerable number of patients with chronic pain can be expected to get long-term relief of pain from TNS treatment, particularly when the etiology of pain is organic, notably neuro-

genic, skeletal or related to superficial structures.

Possible mechanisms responsible for the pain relief from TNS

It has been claimed that pain relief produced by conventional TNS would be a peripheral fatigue phenomenon in nociceptive afferent fibres (Campbell & Taub 1973, Ignelzi & Nyquist 1976, 1979). Since pathways mediating nociceptive and thermal information seem to be similarly organized (see Willis and Coggeshall 1978) we used the thermal sense as a model for nociception, to explore the possibility that TNS really induces central changes.

IV: In eight healthy subjects, changes in threshold values for warm and cold sensation were recorded from the thenar region, during six 35 minute test sessions. During two recordings, conventional or acupuncture-like TNS was given over the ipsilateral median nerve, during two over the contralateral median nerve. Two control recordings were made for each subject, one without any stimulus, one with a period of photic stimulation.

During rest or photic stimulation the warm-cold difference limen never deviated more than 50 % from that seen under baseline conditions. Changes greater than 50 %, evaluated as positive with respect to TNS, were seen in seven of eight subjects, when conventional and/or acupuncture-like TNS was applied. In some subjects, the period of decreased thermal sensitivity considerably outlasted the period of stimulation and in a few, even increased in the poststimulatory period. Interestingly, the changes were seen contralaterally, as well as ipsilaterally, to the stimulation in most subjects. These changes in thermosensitivity during TNS would have to occur via a central mechanism and are a strong indication that TNS can induce long-lasting alterations in the processing of sensory stimuli by the central nervous system. The unchanged thermal limen during control conditions indicate that the increase was not merely due to arousal or distraction.

When pain relief is achieved with either TNS method, there is often a poststimulatory analgesia for several hours. This makes the gate

control theory as such a less likely model for the mechanisms involved. If, on the other hand, the pain relief involved the liberation of a substance with a long half-life like some of the opioid peptides have, the long poststimulatory effect might be explained (see Akil and Watson 1980). Therefore, it was highly interesting to investigate the possible relation between the endogenous opiate system and the two types of transcutaneous nerve stimulation. Furthermore, a study appeared, where the increase in experimental pain threshold in man, induced by needle acupuncture, was reversed by naloxone (Mayer et al. 1977). Since our patients had chronic pain, they represented a clinically more relevant model to test the possible involvement of opioid systems in stimulation-produced analgesia.

III: Twenty chronic pain patients experiencing analgesia from acupuncture-like TNS (10 patients) or conventional TNS (10 patients), since at least three months, were selected for the study. In a double-blind procedure, 4-8 intravenous injections of naloxone or saline were given with 30-60 minute intervals when the patients had analgesia from TNS.

A systematic but partial inhibition of the TNS-induced analgesia was reported by six of the ten patients using acupuncture-like stimulation, implying that opioid peptides participate in pain relief from acupuncture-like TNS. This is in line with the reports of Mayer et al. (1977) on experimental pain. The analgesia from conventional TNS was not consistently reversed in any of the ten patients tested. This observation is an indication against, but does not exclude, the participation of opioid systems in pain relief from conventional TNS, since naloxone may be a less effective opioid antagonist for some subtypes of opiate receptors. Nevertheless, these findings have been confirmed by other workers, who have found no reversal of pain relief from conventional TNS by naloxone in acute (Woolf et al. 1978) or chronic (Abram et al. 1981) pain conditions.

Psychiatric evaluation and outcome of TNS treatment

The seemingly low success rate with TNS in pain with a dominance of psychogenic factors, found by us (I) and others (e.g. Long 1976), appeared to be an aspect which needed further penetration.

V: Consecutive patients who did not experience pain relief from TNS, arbitrarily intermingled with successfully treated patients, were evaluated by a psychiatrist without access to the clinical records. The total number of patients examined were 66. The patients were categorized according to mental illness, pathological personality traits, situational problems, states of reactive mental decompensation and normality. The results were correlated to the outcome of treatment and existence or absence of a relevant organic etiology of the pain.

Psychiatric symptoms occurred in a high frequency both in successfully TNS-treated patients and in failures. However, the symptom profile differed significantly between the two groups. Severely depressed or otherwise psychotic patients as well as those with organic defects or signs of pathological personality traits were found in more than half (28/46) of the consecutive patients in whom TNS failed to relieve pain. The psychiatric diagnosis might well be the major reason why TNS failed. Many of these patients had a relevant physical cause of the pain. It seemed, however, as if the importance of the psychiatric factors diagnosed may have exceeded that of the physical pain, with relation to the outcome of TNS treatment. Patients in this group did after the diagnostic evaluation stay in continuous therapeutic contact with the psychiatric clinic. Situational problems and secondary reactive states, such as anxiety, depression or neurasthenia were common whether TNS treatment had succeeded or failed and seemed unrelated to the outcome of treatment. These symptoms might be expected to fade as the pain condition was brought under control. Patients judged to have no relevant physical cause of the pain were more often treatment failures than patients with a diagnosed adequate organic etiology. Thus, when patients with no observable organic cause of their chronic pain also have signs of mental illness and/or pathological personality traits, these are most likely related to the

perceived pain. It therefore becomes highly unlikely that these patients will benefit from TNS-treatment (cf. V).

Personality aspects related to social adjustment after symptomatic pain relief

In patients with chronic pain, good social (re-)adjustment did not appear to be an inherent consequence of even excellent pain relief with TNS. One explanation might be that personality factors, possibly related to the ego-psychological concept of adaptation, would influence and correlate to social adjustment.

VI: Among patients with a similar and relevant physical etiology of their chronic pain, a selection with reference to social adjustment was made. The patient's mode of acting, ability to work and to live a fairly 'normal' family and community life was evaluated, based on information obtained from medical records and at multiple outpatient visits. Five patients, considered to be well adjusted and five considered to be poorly adjusted were selected. All had satisfactory symptomatic pain relief. Manual and intellectual workers were represented in both groups. The so called 'adaptive capacity' of each individual was assessed with psychological techniques and correlated to social adjustment.

From the test results it was concluded that this small group of patients was a fairly representative sample of the normal population, in the particular respects studied. Seven patients performed well in the cognitive tests and three less well. In the Colour Word Test, five patients had stable response patterns, showing a good adaptation to the particular test situation. In the IES-test, two distinct groups emerged with three patients in each. One group had high id-scores, indicating that they might be considered as 'impulse-ridden' with low 'adaptive capacity'. The other group had high ego-scores and appeared more reflecting and reasoning, disclosing a good 'adaptive capacity'. Four of the patients were more difficult to classify. In the DMT-test, primitive mechanisms of defence, were seen in three patients. When results from all test parameters were added, a prediction of five well adjusted and five poorly adjusted individuals was made. For six patients, the

prediction for social adjustment was correct, i.e. for those with the highest and lowest levels of 'adaptive capacity'. Two of the remaining four were well adjusted, in spite of only mediocre 'adaptive capacity'. The other two were considered poorly adjusted, but showed good adaptive resources in the tests. In these four patients, other factors may have determined what use each individual made of his particular resources for adaptation. Interestingly, in this study, the cognitive performance of the patients did not influence the prediction of social adjustment, suggesting that chronic pain primarily may be an 'emotional' rather than a 'cognitive' problem.

GENERAL DISCUSSION

TNS as a long-term therapy in the relief of chronic pain

There is no better way of eliminating pain than by removing its cause. With any etiological or symptomatic therapy used, however, the efficacy has to be related to the risks involved. When systemically administered drugs are used for symptomatic relief of long-standing chronic pain conditions, the risk for side-effects, physical and psychological dependance and abuse may be considered high (cf. Houde 1980), particularly if pain relief is only partial. Possible complications with nerve blocks or surgical procedures include the reappearance of pain, worse than before (White & Sweet 1969). In symptomatic relief of chronic pain, TNS earns its clinical value from being easy to handle by the patient, administered at his own responsibility and from being a technique almost totally void of side-effects and complications.

In our hands, TNS was particularly efficient in relieving pain considered to have a relevant organic etiology, particularly when localized to skeleton, joints or due to peripheral neurogenic lesions, many of which caused radiating pain (I, II). Other authors, employing conventional TNS only, have arrived at similar conclusions (Table 4). Bates and Nathan (1980) found 40-45 % of 235 patients with chronic pain to have useful pain relief after one month. There were 74 patients with postherpetic neuralgia and several with chronic back pain, amputation stump pain, painful scars and pain due to peripheral nerve lesions. Sindou and Keravel (1980) reported on the use of conventional TNS in 180 patients with chronic pain due to neurological disorders. In peripheral nerve lesions (55 patients), good or excellent pain relief was achieved in 87 % and in postherpetic neuralgia (34 patients) in 67 %. Those peripheral nerve lesions with signs of increased sympathetic activity, also seem to respond well to TNS (Bohm 1978). The variations in success rate between different authors may, at least partly, be due to differences in the primary selection.

We found TNS to be one valuable alternative for chronic pain in the trigeminal region (II), with more than 50 % of the patients having useful pain relief at three months observation time. Gregg (1978) reported that 6 of 33 patients with posttraumatic facial pain were markedly relieved by conventional TNS. Most likely, the addition of acupuncture-like TNS is one important factor for our better results (cf. Ihalainen and Perkki 1978). In contrast, Bates and Nathan (1980) noted particularly poor results with pain localized to the face. One reason mentioned was that many of their patients found the electrodes and connections to be a conspicuous and unacceptable social handicap.

In the small number of patients with pain of central origin, we found TNS to be most effective when the pain had a suprasegmental etiology, e.g. thalamic pain, or was localized to the level of a spinal lesion (cf. Davis & Lentini 1975, Hachen 1977-78). Wynn Parry (1980) reported conventional TNS to be a valuable addition to other available therapies in chronic pain due to avulsio of the brachial plexus. Other authors (e.g. Bates & Nathan 1980, Sindou & Keravel 1980) have pointed to the poor results with pain due to lesions in the central nervous system. The disagreement seems to be a matter of how success rates are looked at. Even if the success rate is 'only' 10-30 % in central pain (cf. Sindou & Keravel 1980), TNS may make a tremendous difference to those particular patients, who are helped. Since there are no risks involved, a rather generous attitude towards indications for a TNS trial, seems justified.

We chose to judge the TNS trial as a success or failure after three months observation time. After an initial trial period of this length, few patients discontinued TNS treatment up to two years (I, II). Interestingly, Sindou and Keravel (1980) found the long-term results to vary in different etiological groups. Among patients with peripheral nerve lesions success rates decreased only slightly during three years whereas among patients with postherpetic neuralgia, the successfully treated group of patients was decreased to 25 % within one year (cf. Bates & Nathan 1980). The steep fall over time in success rates, i.e. the poor long-term results, observed by

several authors (Tables 1 and 4) may, at least partially, be an effect of a too short initial trial period. However, this may be a practical necessity when stimulators are not free of charge, as in Sweden.

The addition of acupuncture-like TNS has significantly improved the overall results as compared to conventional TNS only (Table 1 and 4). Acupuncture-like TNS might be of particular value when cutaneous sensitivity is impaired (I, cf. Wynn Parry 1980, Sindou & Keravel 1980), although this question is not finally settled (II). When the afferent pathway by which conventional TNS activates pain controlling systems is damaged, an effect seems less likely. This might be an argument against the use of destructive methods for relief of chronic pain of benign origin, before the non-invasive TNS techniques have been tried.

TNS is most certainly a treatment which initially gives the patient much personal attention. Suggestion, anticipation of relief, diminished anxiety and a wish to please the therapist are factors which might play a role in ameliorating pain, particularly in the short-term perspective. Interestingly, placebo meditation is approximately ten times more effective in relieving clinical pain than experimental pain (Beecher 1960). Any medical treatment, delivered with authority, enthusiasm and much personal care will for a limited time effectively relieve pain in approximately one third of the patients (Thorsteinsson et al. 1978, cf. Beecher 1959). It has been assumed that this placebo response is a type of suggestion. However, no consistent relation has been found between suggestibility and placebo response (see Evans 1974).

Thorsteinsson and co-workers (1978), in a prospective study found the relief of chronic pain from conventional TNS to be significantly greater (48 %) than pain relief from placebo stimulation without

batteries (32 %), (cf. Ihalainen & Perkki 1978). The fact that TNS was a most unsuccessful treatment for pain of predominantly psychogenic origin (I, V) also suggests a mechanism of pain relief affecting peripheral ascending pathways related to somatic nociception. Furthermore, clinical observations on the varying effectiveness of different electrode positions (own observations, e.g. Ebersold et al. 1975) and the necessity for a stimulation strength producing paresthesiae (e.g. Wall & Sweet 1967) and muscle contractions (I) respectively, imply that a physiological mechanism is involved in pain relief from TNS.

With a long follow-up time, the rate of treatment efficiency is probably recorded more accurately (Loeser et al. 1975, Long 1979), although there is always an increased risk of false therapeutic claims in diseases with a spontaneous course, characterized by periods of remission, e.g. chronic facial pain (II). However, also in this respect, a follow-up time of two years, as used in our study, may be regarded as satisfactory for a therapeutic evaluation of the treatment used.

Artificial activation of endogenous pain control systems, at present seems to be the most rewarding approach to symptomatic relief in chronic pain. However, even when patients with pain mainly due to psychogenic factors were excluded, approximately half of the patients referred to our pain unit, did not experience pain relief with TNS in the long run. One reason may be that the pain was qualitatively or quantitatively unresponsive to the rather narrow range of stimulation parameters used. Another, that the particular pain-controlling mechanisms activated by conventional and acupuncture-like TNS, in these patients were more difficult to activate.

Possible mechanisms of action of TNS

It has been claimed that high frequency TNS might involve excitability changes of the peripheral nociceptive fibres (Campbell & Taub 1973, Ignelzi & Nyquist 1976, 1979). However, neither conventional nor acupuncture-like TNS is painful. Furthermore, cutaneous thresholds to nociceptive heat, measured in man during non-painful percutaneous stimulation of sensory nerves, increased in, as well as outside, the distribution area of the stimulated nerve (Hiedl et al. 1979). In normal subjects, the temperature sensitivity decreased bilaterally during and after unilateral stimulation with non-painful conventional or acupuncture-like TNS (IV). Furthermore, both types of TNS seem effective in relieving pain conditions of central as well as peripheral origin (I, II). Thus, the analgesia is most likely evoked by central mechanisms.

One possible locus for the central interaction is the dorsal horn at the segmental level of stimulation. The gate control theory has frequently been used to explain the analgesic effects. As discussed earlier, results from experimental studies do not, however, correspond with all aspects of the clinical effects seen. So far, there is no clear evidence that either conventional or acupuncture-like TNS activates a 'gate' of the Melzack-Wall model.

Clinical as well as experimental data suggest different mechanisms of action for conventional and acupuncture-like TNS. The time needed to induce pain relief by conventional TNS was usually shorter (5-15 minutes) than by acupuncture-like TNS (15-30 minutes), (Eriksson and Sjölund 1976). Correspondingly, the changes in tooth pain threshold after electroacupuncture differed from those after high frequency stimulation (Andersson et al. 1973, Andersson & Holmgren 1978). With electroacupuncture the threshold slowly rose and slowly returned to baseline, whereas the increase with high frequency stimulation was rapid and transient. There are also differences in the clinical usefulness of the two techniques. When skeleton or joints are involved, conventional TNS seems more effective, whereas when pain is radiating or related to muscle

tissue, acupuncture-like TNS more often releases it. When hypesthesia was noted in the area of pain (I), the proportion of patients with analgesia from acupuncture-like TNS increased. Thus, it seems as if the mechanism responsible for analgesia in conventional TNS cannot easily be activated via deep structures. Similarly, the fact that muscle contractions are necessary for analgesia by acupuncture-like TNS, indicates that the mechanism responsible cannot easily be activated via cutaneous afferents. It is not known exactly what afferent input underlies the pain-relieving effect of either method. Acupuncture-like stimulation activates alfa motor neurons, with possibilities of interneuronal activity secondary to antidromic spread. Since the large myelinated muscle afferents are similar in size to alfa motor neurons, they may also be activated. Moreover, via the muscle contractions, small and/or large afferent fibres may be activated via the receptors in the muscle(s).

The naloxone study (III) suggested that acupuncture-like but not conventional TNS acts through links utilizing endorphins (cf. Abram et al. 1981). The partial effect of naloxone on pain relief from acupuncture-like TNS (III) may imply that the doses were insufficient and for example antagonized mu-receptors but not delta-receptors on primary afferent fibres (Fields et al. 1980) or that a more complicated mechanism was involved. Since naloxone was given systemically it was not possible to say at what level of CNS the action took place. However, measurements of endorphin activity in lumbar cerebrospinal fluid in pain patients experiencing pain relief from acupuncture-like TNS showed an increase only when the patients received treatment, which activated muscles with lumbo-sacral innervation (Sjölund et al. 1977). This indicated the participation of a segmental opioid mechanism in pain relief by acupuncture-like stimulation. This opioid mechanism might be activated directly or via brain stem mechanisms.

TNS therapy and psychiatric symptoms

Pain is often regarded as indicative of organic disease. It is also, however, a common sign in psychological disturbance or psychiatric illness. Interestingly, over 60 % of the patients in a psychiatric clinic complained of pain (Klee et al. 1959). Furthermore, primarily organic pain is commonly associated with reactive emotional and psychological changes (see Merskey and Spear 1967). Among patients who were consecutive TNS failures, symptoms of mental illness or psychological disturbances were seen in 70 % (V).

When the patient has had chronic pain for a relatively short time, it may not be an easy task to separate what part of the pain experience is a consequence of increased input in nociceptive pathways and what part is emotionally determined. As the negative records from successive diagnostic investigations add up, the diagnosis of pain due primarily to mental factors becomes easier. However, it is valuable to assess the relative importance of organic and psychogenic etiological factors at an early state. As would be expected, therapeutic approaches, other than TNS, have proven more efficient when the cause of pain is predominantly mental. A correct early diagnosis might also prevent some unnecessary, costly and potentially harmful diagnostic procedures.

Since psychological/emotional causes of pain are common and since an etiological diagnosis seems to be the most useful predictor for the outcome of TNS treatment (cf. Johansson et al. 1980), the usual somatic investigation in chronic pain needs a psychiatric complement, early in the disease process. When the etiology of pain is primarily organic and the mental symptoms diagnosed are of the reactive type, the outcome of TNS treatment seems unrelated to the psychiatric symptoms (V). On the other hand, when there are signs of mental illness or pathological personality traits, TNS, as well as other somatic treatments, will most likely fail to relieve the pain, whether there is a relevant organic core or not.

Symptomatic pain relief and successful social adjustment

In acute pain the therapeutic goal is complete pain relief. In chronic pain of benign origin, total relief of pain is often an unrealistic goal as evidenced by these patients' extensive histories of prior treatment failures. The primary purpose of treatment is then social adjustment, if possible including continued activity in a previous or new occupation (cf. Newman et al. 1978). Unfortunately, significant symptomatic pain alleviation by itself is not sufficient to rehabilitate all chronic pain patients. Personality factors as well as environmental ones influence the outcome, particularly it seems when the pain condition has a long duration (Maruta et al. 1979, cf. Black 1975).

The personality factors relevant to social adjustment in chronic pain has, however, not been identified. Our hypothesis was that the concept of adaptation in psychoanalytic terms, a reciprocal relationship of the organism and its environment, would be of relevance. More precisely, we believed that the various aspects of 'adaptive capacity' measured, would be a good predictor of social adjustment. The results imply that our hypothesis was too simple, granted that our small sample was representative of a larger pain patient population. However, this type of psychological evaluation technique may still be useful as an early prognostic tool in pain, threatening to become chronic. One might presume that patients found to have good adaptive resources will readjust well to society with little or no therapeutic aid. On the other hand, patients with low 'adaptive capacity' might not be able to adjust in spite of maximal support. Thus, when the therapeutic resources are limited they may be most efficiently used among patients with intermediate 'adaptive capacity', where other factors may have a decisive influence on social adjustment in a chronic stress situation such as pain.

From a physician's point of view, different levels of 'adaptive capacity' are difficult to recognize. One would believe that anamnestic flexibility and proof of good adjustment in earlier stress situations as well as a general reflecting, reasoning attitude with a realistic orientation to the future, would be indications of a high level 'adaptive capacity' whereas for example rigidity, unrealistic expectations on hospitals and physicians as well as uncontrolled impulsive acting would indicate a low level. This might be true in general terms, however, in one of the patients with intermediate 'adaptive capacity', pronounced rigidity was most likely the factor which made him keep his earlier patterns of good social behaviour. Also in patients undergoing chronic hemodialysis, rigidity showed a positive correlation to good adjustment (Hagberg 1974). Reports from so called multidisciplinary pain clinics (Newman et al. 1978, see also Hallett & Pilowsky 1982) indicate that the general therapeutic attitude towards the problem of chronic pain is likely to influence treatment results. This might be particularly true for the group of patient's with intermediate 'adaptive capacity'.

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Epilogue

Patients in pain often consider the pain to be caused by a pathological process, over which they have no control. The reason for this is most likely that our medical society believes in an analytical disease model, which tends to demand one pathophysiological etiology for any constellation of symptoms. This rather narrow approach has nevertheless had tremendous scientific and medical success and thereby put aside other alternatives. When chronic pain is defined only by somatic parameters, many physicians will not be concerned with psychosocial issues. There is an old saying in traditional Chinese medicine: "When the whole gets better, the disease will improve". Optimal recovery in long-standing pain, as in other chronic conditions, may for many patients be accomplished only if the influence of non-somatic factors on the pain condition is appreciated.

CONCLUSIONS

TNS gives pain relief to a significant number of patients with chronic pain of benign origin.

Acupuncture-like TNS is a useful additional therapy for patients unresponsive to conventional TNS and accounts for at least one third of the total success rate.

A positive TNS effect seen after 3 months usually lasts at least for 2 years.

TNS is most effective when the etiology of the pain condition is organic, notably neurogenic, skeletal or localized to superficial structures.

TNS is an alternative to neurosurgical procedures for intractable facial pain, particularly in the elderly and when pain is 'atypical'.

An etiological diagnosis, somatic or psychiatric, is the best predictor for the outcome of treatment. When TNS does not relieve pain the probability of a psychiatric/psychological etiology is high.

A psychological evaluation may be of value in predicting social adjustment in patients successfully treated with TNS.

The mechanisms responsible for pain relief from TNS are probably central and for acupuncture-like TNS, at least partially mediated via opioid systems.

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LONG TERM RESULTS OF PERIPHERAL CONDITIONING STIMULATION AS AN ANALGESIC MEASURE IN CHRONIC PAIN

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SUMMARY

In the present study 123 patients with chronic pain, consecutively referred for symptomatic pain treatment, were given peripheral conditioning stimulation as an analgesic measure and were followed for 2 years or till they terminated the treatment. The stimulation was either conventional transcutaneous nerve stimulation (TNS) [35] of mainly cutaneous afferents with high frequency (10–100 Hz) or acupuncture-like TNS [11] where muscle nerves are activated at a low repetition rate (1–4 Hz) with small trains of stimuli. The follow-up showed that 55, 41 and 31% of the patients continued the treatment after 3, 12 and 24 months, respectively. About 30% of the patients had to use acupuncture-like TNS to get useful analgesia, defined as a desire of the patient to continue stimulation treatment. Three-quarters of the successfully relieved patients reported more than 50% pain relief as measured from visual analogue scales and half of these reported an increased social activity and a decrease of analgesic drug intake by more than 50%. Psychogenic and visceral pains were less suitable for TNS treatment. It is concluded that peripheral conditioning stimulation is a valuable therapy in cases of chronic pain and that both conventional and acupuncture-like TNS should be tried before considering implantable devices or destructive surgery.

INTRODUCTION

During the last decade conditioning stimulation of peripheral nerves with electrical pulses given transcutaneously (transcutaneous nerve stimulation; TNS) and direct stimulation of presumably mainly the dorsal columns of the

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spinal cord via implanted electrodes (dorsal column stimulation; DCS) have been increasingly used to produce analgesia in patients with chronic pain. This therapy emerged from the gate theory of Melzack and Wall [21] in which it was postulated that activity in coarse primary afferent fibres mainly mediating touch would lead to presynaptic inhibition in the dorsal horn of the activity in thin afferent fibres, mediating pain. The experimental data behind this theory (e.g. ref. 22) have been shown to be partly wrong (see ref. 28). However, there is evidence that dorsal horn neurones, activated by noxious C-fibre input and possibly mediating pain centrally, are inhibited by activation of coarse myelinated nerve fibres [15]. Moreover, several authors have reported that a clinically useful analgesia can be produced by high frequency stimulation of peripheral nerves at an intensity evoking activity chiefly in coarse myelinated fibres (Fig. 1A) [18,19,23,29,35]. Few follow-up studies have been published but it seems that in the hands of others as well as in ours this stimulation method is effective only in a minority of patients with chronic pain [18-20, cf. however 27].

To improve the results of peripheral conditioning stimulation for analgesia, we recently developed a new kind of such stimulation [11] where experiences from the Chinese electro-acupuncture were utilized. With electro-acupuncture, high intensity electrical pulses are given via the inserted needles, usually at a low frequency of about 1–2/sec (Fig. 1B) [2,17]. Surgical procedures may be performed with electro-acupuncture as the only analgesic measure [6,17] and in healthy volunteers the threshold for experimental tooth pain was found to rise [2,8,16]. Furthermore, stimulation of deep afferents was reported to be essential for the effect [9], whereas surface electrodes could be substituted for the needles provided that strong muscle contractions were elicited in segmentally related myotomes [4]. When tried clinically, patients with chronic pain generally did not tolerate the stimulation strength necessary to elicit strong muscle twitches near the painful area [3]. However, when we substituted a brief train of impulses for the single impulse (Fig. 1C) it was possible to decrease the stimulation strength to tolerable levels, maintaining the muscle twitches and the induction of analgesia in patients with chronic pain resistant to conventional high frequency stimulation [11,12].

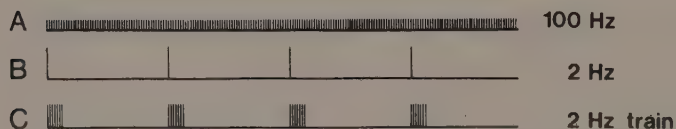


Fig. 1. Different methods of peripheral conditioning stimulation for the induction of analgesia. A: continuous barrage of brief monophasic pulses as in conventional high frequency TNS. B: single brief monophasic pulses given at a low frequency as in electro-acupuncture. C: short trains (100 Hz internal frequency, duration 70 msec) of brief monophasic pulses given at a slow repetition rate as in acupuncture-like TNS. Note the differences in intensity (relative pulse amplitude) necessary for the induction of analgesia with the 3 types of stimulation.

In the present report we describe the results of a 2 year follow-up of 123 patients with chronic pain treated with either type of peripheral conditioning stimulation. All the patients first tried conventional high frequency stimulation and if the analgesia was not sufficient, they were instead treated with acupuncture-like low frequency train stimulation. As will be shown, the compiled results were then improved as compared to those of conventional TNS alone. Furthermore, peripheral conditioning stimulation appears to be a valuable tool in the long term treatment of chronic pain.

METHODS

The study was performed on those patients consecutively referred during 18 months to the pain treatment group of Lund University Hospital for symptomatic pain treatment. We have excluded 6 patients who died from their pain causing disease within 1 week, 2 patients who needed aetiological therapy and one patient who moved abroad and could not be followed. The age distribution of the remaining 123 patients is shown in Fig. 3A (median age 61 years) and the sex distribution was 78 males and 45 females.

Stimulation treatment was given according to a fixed schedule in our open care unit by two of us (M.E. and B.S.). The patient was first subjected to a neurological examination and then conventional high frequency stimulation was performed during a long session with several electrode locations. If some analgesia was reported the patient was allowed to try the stimulation at home for 1–2 weeks and to vary the stimulation frequency within the 10–100 Hz range to get the best results. If no analgesia was reported at the first session or was insufficient after the initial trial period, the patient was instead given acupuncture-like stimulation during another long test session, care being taken to produce strong muscle twitches in myotomes segmentally related to the painful area. If after another trial period at home this stimulation did not produce analgesia, the patient was excluded from further stimulation treatment and was registered as a failure. If the stimulation treatment did produce *useful analgesia*, defined as a desire from the patient to continue the treatment, the patient received his own stimulator and was seen with regular intervals for 2 years or until the treatment was terminated. In addition, all patients with no physical signs of somatic disease and negative laboratory tests (diagnostic radiology, electromyography), as well as those who never reported any useful analgesia, were referred to a blind psychiatric evaluation by one of us (S.N.). After 3 months of treatment all the patients still using stimulators filled in questionnaires and scored their pain intensity on a visual analogue scale [26] before and after stimulation. They were also asked how often they used the equipment, about their previous and present analgesic intake and about possible changes in their social activity after stimulation.

The stimulator used (Fig. 2) is a portable constant current unit that delivers monophasic square wave pulses of 0.2 msec duration at maximally 60 mA into a load of 2500 Ω , manufactured according to our specifications

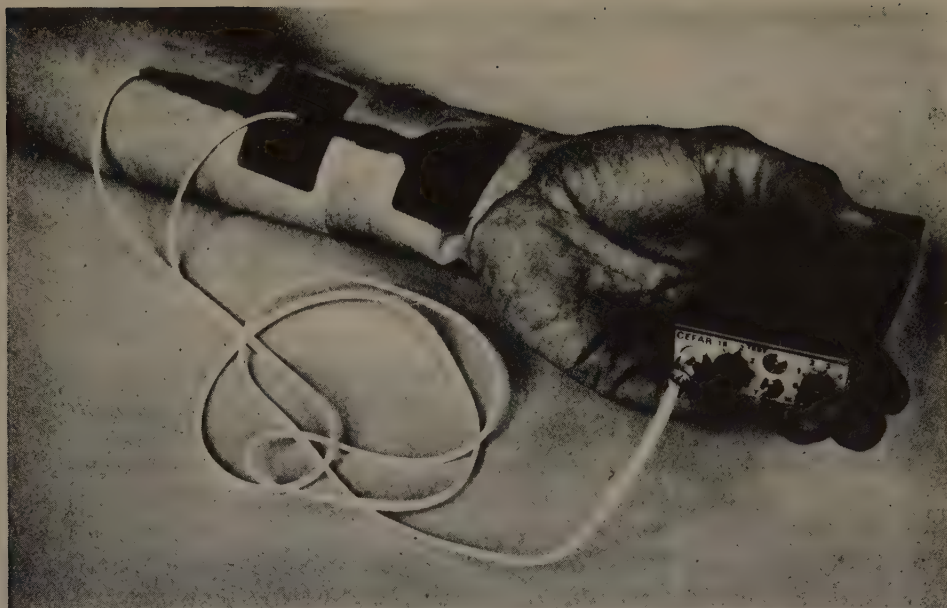


Fig. 2. Portable constant current stimulator for conventional and acupuncture-like TNS. Carbon rubber electrodes over median nerve. See text.

(CEFAR Medical Products, S-222 27 Lund, Sweden). Both conventional high frequency TNS (10–100 Hz; Fig. 1A) and acupuncture-like low frequency TNS (train duration 70 msec and internal frequency 100 Hz; repetition rate 1–4 Hz; Fig. 1C) can be produced. The stimulation was given via standard carbon rubber electrodes size 14 cm² (Fig. 2), coated with conducting gel and placed within or around the painful area or over nerve branches innervating the painful dermatome (conventional TNS) [25] or the corresponding myotome (acupuncture-like TNS). The stimulation intensity was 2.5–3 times the perception threshold in conventional TNS (usually 12–30 mA) and 3–5 times the perception threshold in acupuncture-like TNS (usually 15–50 mA; cf. Fig. 1) [11]. The duration of stimulation was initially 30 min, 3 times daily and then varied according to individual needs (cf. Results).

RESULTS

From the histogram of Fig. 3B it appears that out of the 123 patients given stimulation treatment (hatched bar) 68 patients (55%) continued the treatment after 3 months, 50 patients (41%) continued after 1 year and 38 patients (31%) continued after 2 years. In these numbers are included 6 patients who died between 1 and 3 months after the start of stimulation, 4 patients who died between 3 and 12 months after the start of stimulation

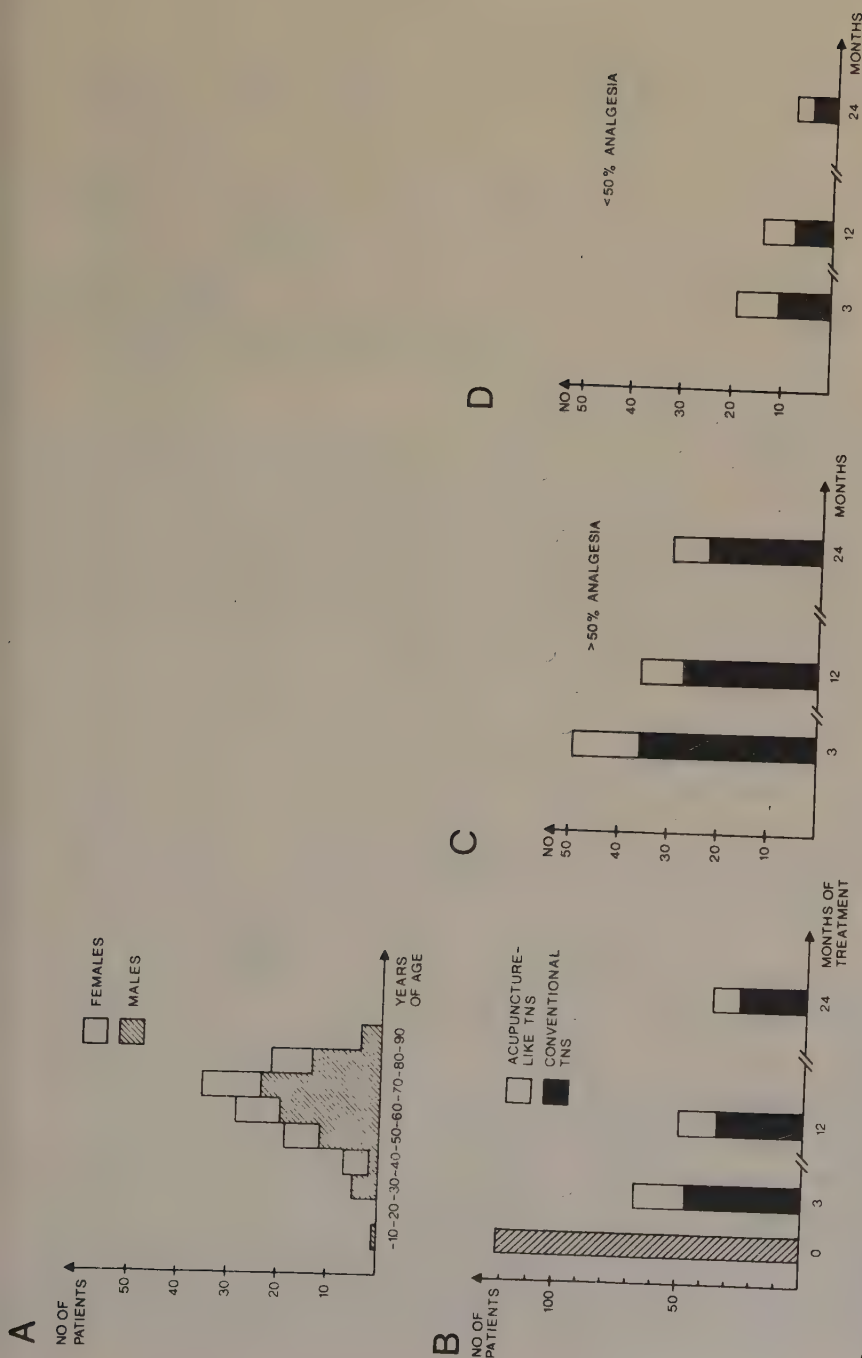


Fig. 3. A: age and sex distribution of the patients with chronic pain in this study. B: number of patients starting (oblique hatching) and continuing stimulation treatment after 3, 12 and 24 months. Type of stimulation according to key. C: patients indicating more than 50% analgesia on visual analogue scales after stimulation, at indicated times. D: patients indicating less than 50% analgesia on visual analogue scales after stimulation, at indicated times.

and 3 patients who died between 1 and 2 years of stimulation, all with useful analgesia till their deaths.

Why did some patients discontinue the stimulation treatment? In Fig. 4 the main causes are listed in relation to the duration of the treatment. From these histograms it is apparent that most of the patients who discontinued the treatment did so within the first 3 months, mainly because they never experienced useful analgesia, whether due to somatic (Fig. 4A) or psychogenic (Fig. 4C) factors [24]. Only a few patients interrupted the stimulation treatment because of difficulties to cope with the technique (Fig. 4B) or due to the development of tolerance (Fig. 4E). Out of those who discontinued due to changes in pain intensity, 6/12 had experienced a spontaneous decrease of the pain since the start of the treatment (Fig. 4D).

As concerns the degree of pain relief scored after 3 months on a visual analogue scale, the majority (72%) of patients with useful analgesia indicated more than 50% pain relief (Fig. 3C), whereas only 28% indicated less than 50% relief (Fig. 3D). Interestingly, after 24 months the proportions were approximately the same, 79% versus 21%.

Aetiological factors and the location of pain influenced the results as can be seen from Table I. Here the patients are grouped according to these variables in relation to how many of them that continued the treatment after 3 months, i.e. when the patients who never experienced any useful analgesia had discontinued the treatment (Fig. 4). It is evident that neuralgia, especially in the face (group 1a; atypical and typical trigeminal neuralgia) [cf. 13] but also at other locations (group 1b) could often be controlled with

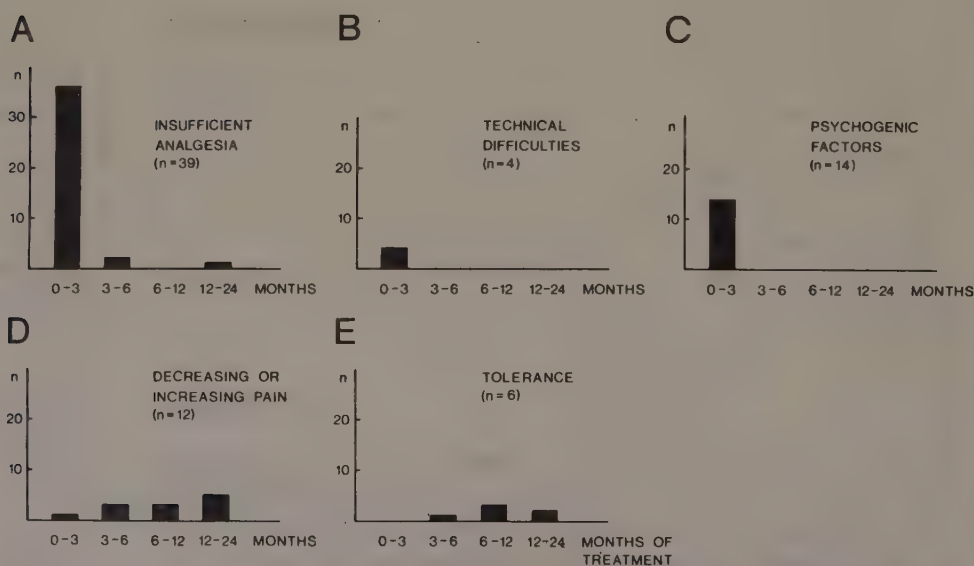


Fig. 4. A-E: main reasons for interrupting stimulation treatment after times indicated. n = number of patients.

TABLE I

NUMBER OF PATIENTS STARTING STIMULATION TREATMENT AND CONTINUING AFTER 3 MONTHS, GROUPED ACCORDING TO CAUSE (AND LOCATION) OF PAIN

() = patients using acupuncture-like TNS. See text.

Cause (and location) of pain	Starting treatment	Continuing after 3 months
1. Neuralgia		
(a) in face	11	9 (1)
(b) in other locations	32	18 (4)
2. Rhizalgia	22	14 (8)
3. Dorsalgia	7	6 (—)
4. Centrally evoked pain	18	12 (6)
5. Cancer pain		
(a) in parietal structures	6	4 (—)
(b) in visceral structures	5	1 (—)
6. Ischaemic pain in extremities	5	1 (1)
7. Psychogenic pain	17	3 (1)
In total	123	68 (21)

peripheral conditioning stimulation. The latter group consisted of patients with neuralgia due to both trauma, inflammatory and metabolic disorders. Also rhizalgia (2 cervical, 20 lumbar) and dorsalgia could often be relieved (groups 2 and 3). In the case of pain due to a lesion of the central nervous system (group 4), 5/7 patients with damage rostral to the spinal cord and 7/11 with damage to the spinal cord and roots experienced useful analgesia of which 6/7 of the latter had pain at the level of the lesion. Concerning cancer pain it was in 4/6 cases possible to relieve considerably the pain of metastasis to the skeleton (group 5a) but not as a rule that due to cancer growth in visceral structures (group 5b). Neither was treatment of ischemic pain very successful (group 6) even if the number of patients is limited. Finally the pain of patients with no objective signs of somatic illness and a positive psychiatric evaluation, i.e., probably psychogenic pain (24) did not as a rule respond to stimulation treatment (group 7).

Certain factors were found to be relevant to the choice of stimulation method, i.e., when to use acupuncture-like TNS or conventional TNS. From the histogram in Fig. 3B it can be seen that acupuncture-like TNS alone was effective in almost one-third of cases, both after 3 (32%), 12 (30%) and 24 (29%) months of treatment, implying an improvement by more than 40% of the compiled results of stimulation treatment over conventional TNS only. The new method was of particular value in rhizalgia and in some cases of neuralgia and centrally evoked pain (Table I). Prior treatment in the form of destructive surgery (neurotomy, rhizotomy, cordotomy, injection of neurolytic agents) had been performed in 14/15 cases relying on acupuncture-like TNS but also in most cases using conventional TNS after 1 year (Fig. 5B). However, all the patients helped only by acupuncture-like TNS

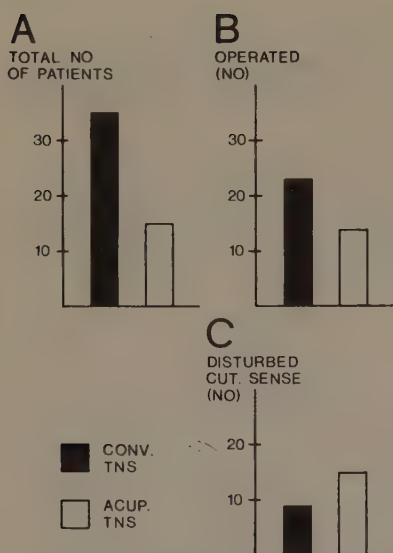


Fig. 5. A: total number of patients continuing treatment for 1 year. B: number of patients on which destructive surgery had been undertaken. C: number of patients with hypaesthesia in and around painful area. Bars according to key.

had a cutaneous hypaesthesia in and around the painful area whereas this was so only in a minority of cases (9/35) using conventional TNS (Fig. 5C).

How did the stimulation treatment influence the life of a patient with chronic pain? In Table II, data from 50 patients using the treatment more than 1 year are shown. Among the patients with more than 50% pain relief 16/36 had substantially decreased their intake of analgesics and 18/36 had increased their social activity [cf. 19]. On the other hand, in spite of about as frequent use of the stimulation treatment, those patients reporting less than 50% pain relief only rarely (2/14 cases) decreased their analgesic intake and became more active.

TABLE II

QUESTIONNAIRE DATA FROM 50 PATIENTS ON STIMULATION TREATMENT FOR 1 YEAR

() = patients using acupuncture-like TNS. See text.

Degree of pain relief	Number of patients	Number of stim./day		Analgesic intake			Increased social activity
		≤4	>4	Never used	Decrease		
					>50%	<50%	
>50%	36 (9)	21 (7)	15 (2)	5 (2)	16 (3)	15 (4)	18 (3)
<50%	14 (6)	10 (4)	4 (2)	3 (—)	2 (2)	9 (4)	2 (1)

As to side effects of the stimulation treatment 15 of our 123 patients at some time reported erythema and irritation of the skin, which however, cleared in a few days after temporary withdrawal of the stimulation. Relapses could usually be avoided by proper skin and electrode care, particularly by maintaining the layer of conducting gel intact. Serious allergic reactions of the skin were seen in 2 patients, who could continue treatment after switching to damped foam rubber electrodes. Three patients (all with post-irradiation neuropathy after mammary neoplasm) increased their lymphoedema in the painful arm after stimulation which subsided after cessation of treatment. Eighteen patients, none of whom continued the treatment, reported a temporary increase in pain intensity after stimulation [cf. 25]. Nine of these had a positive psychiatric evaluation [24].

DISCUSSION

It is evident from the present 2 year follow-up that peripheral conditioning stimulation is a powerful method to combat chronic pain in many cases. In our material 55% of the patients benefitted from the stimulation treatment after 3 months, 41% after 1 year and 31% after 2 years. Our results are thus superior to those of Ebersold et al. [10], who reported that 35% of their 230 patients had a useful analgesia after a mean observation time of 3.5 months, of Cauthen and Renner [7] who reported useful analgesia in 32% out of 113 patients after 1 month and of Loeser et al. [18], who reported that only 12.5% of their 198 patients stayed on stimulation treatment for 1 year. From a letter survey sent to 5 major pain treatment centres in the United States with experience from 3000 patients, Long and Hagfors [20] reported that 25–30% of these patients found the stimulation treatment of considerable value but no observation time was stated. On the other hand, approaching our results, Long [19] described the results of 197 patients "leaving the hospital with a device", where 75 patients (38%) felt that their stimulation treatment was adequate after 1 year. However, since these patients were all willing to try stimulation at home, a positive selection might have been introduced in his material as compared to ours. Even more outstanding are the results of 396 patients on stimulation treatment for an average time of 7 months reviewed by Ray [27], who claimed that about 60% of the cases experienced >50% pain relief. It is not clear from his report, however, how many patients originally tried the treatment.

Obviously, the present discrepancies are partly due to the selection of the patient material and to the definitions of success and failure of the treatment. It is interesting, however, that if we disregard the patients helped by acupuncture-like TNS and look at the results of conventional TNS alone in our study, performed much as in the above mentioned reports, the number of patients experiencing useful analgesia decreases by about 30%. This means that 40% of the patients would continue after 3 months, 29% after 1 year and 21% after 2 years. We therefore find it essential to try both types of conditioning stimulation before turning to implantable devices or destructive surgery.

Concerning the reasons for discontinuing the treatment, it is first of all evident that conditioning stimulation is not a suitable method for the treatment of psychogenic pain (Table I, Fig. 4C). This is in accord with the experience of other authors [18,19]. In this context it is interesting that patients with somatogenic pain have a low content of one endorphin fraction in the lumbar cerebrospinal fluid [32] while those with psychogenic pain have normal or even supernormal contents [1].

Another substantial group of patients who did not continue the treatment were those who never experienced useful analgesia. Among these were 14/32 cases of neuralgia of the body [cf. 5], whereas those with neuralgia of the face had a better outcome [13]. In spite of a marked improvement of the compiled results on cases with rhizalgia by the acupuncture-like TNS, still 8/22 patients never experienced useful analgesia. Both the failures in this group and those in the group of centrally evoked pain (6/18 cases; Table I) might be due to a lesion of the afferent pathway normally activated by the conditioning stimulation. A corresponding mechanism would explain the fact that cutaneous hypaesthesia was much less common in the cases using conventional TNS, that presumably employs activation of cutaneous afferents, than in the cases who had to use acupuncture-like TNS, that probably employs activation of deep afferents (Fig. 5C) [9]. The reason for the failure in pain of visceral origin (4/5 cases) is not clear but might be due to a different organization of the visceral pain afferents at the segmental level, peripheral conditioning stimulation having no access to their control circuits.

It could be argued that much of the analgesic effect or peripheral conditioning stimulation is due to the placebo effect, which has been reported to be about 33% on a short term basis for any treatment [18]. However, the present results indicate a 55% success rate at 3 months and a 41% success rate at 12 months, which is hardly explainable as a placebo analgesia considering that most of these patients have tried many other types of treatment without even short term success. Furthermore, Thorsteinsson et al. [34], while finding analgesia in 32% of trials on placebo stimulation, reported analgesia in 48% of trials with conventional TNS in a double-blind cross-over short term study. As regards the acupuncture-like TNS, the analgesia produced has been reversed by the narcotic antagonist naloxone in a double blind study [30] and a local increase of the endorphin content in the cerebrospinal fluid has been found after stimulation [32], which points to a genuine stimulation-evoked effect.

Is there any difference in analgesic effect between the two types of stimulation? Due to the design of this study many patients did not try acupuncture-like TNS and therefore a true comparison cannot be made. From the visual analogue scale data (Fig. 3C-D) it appears that in the group indicating a more than 50% relief acupuncture-like TNS was used in only 1/4 of the cases while in the group with less than 50% relief it was used in about half the cases. However, this could be due to that those who had a relief of less than 50% had a more intense pain that was more difficult to treat. Thus they more often did not succeed with conventional TNS and turned to the second

choice, the acupuncture-like TNS. The comparison made between "transcutaneous electrical stimulation" and classical needle acupuncture by Fox and Melzack [14] is unfortunately also difficult to evaluate since they used essentially a low frequency, acupuncture-like stimulation as transcutaneous stimulation. However, the fact that some of our patients got relief from acupuncture-like TNS but not from conventional TNS (Fig. 3B) implies either that the analgesia from acupuncture-like TNS is more effective or that the two methods have different mechanisms of action. The latter possibility is supported by the fact that the analgesia from acupuncture-like TNS but not from conventional TNS is reversed by naloxone [31] and that they probably utilize different afferent channels [4,9] (Fig. 5 of the present paper). Furthermore, whereas the induction time for analgesia is very short with conventional TNS (often 2–10 min), it is 20–30 min with acupuncture-like TNS [11], allowing a substance (endorphin?) to be released or secreted into cerebrospinal fluid [32]. There is also a tendency for patients to use the acupuncture-like stimulation with longer intervals than the conventional stimulation (11/15 cases versus 20/35 cases less than 4 times a day, Table II), inferring a long lasting analgesia which could be caused by a slow elimination of an active principle. On the other hand, the analgesia induced by conventional TNS may sometimes last for several hours [11,19] which is not readily explained by a theory involving ordinary (pre)synaptic inhibition [21].

In conclusion, the present study emphasizes that peripheral conditioning stimulation with conventional or acupuncture-like TNS represents a valuable long term therapy in chronic somatogenic pain, that this therapy can substantially reduce the analgesic intake and increase the social activity of previously incapacitated patients [cf. 33] and that both stimulation methods should be tried before implantable devices or destructive surgery are considered.

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PAIN RELIEF FROM PERIPHERAL CONDITIONING STIMULATION IN
PATIENTS WITH INTRACTABLE FACIAL PAIN

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ABSTRACT

In a prospective study, 50 consecutive patients, referred to a pain treatment unit for surgery due to various forms of facial pain, were all given TNS therapy and followed for two years. Six patients left the study but of the remaining 44, 20 (45 %) reported satisfactory analgesia from conventional or acupuncture-like TNS at the two year follow-up. The latter technique markedly improved the overall results. No serious side effects were seen. 'Atypical facial pain' of known etiology responded best to treatment but also with 'tic douloureux' satisfactory relief was often produced. Duration of the pain condition as well as sex of the patient were predictors of treatment results. It is concluded that TNS therapy represents a valid alternative to surgery when pharmacological therapy fails, especially in the elderly and in patients with atypical pain.

INTRODUCTION

Patients with chronic, so called intractable facial pain (IFP) may present therapeutical problems. This is true for typical trigeminal neuralgia ('tic douloureux') as well as for atypical forms of facial pain (e.g. Rasmussen 1965, Loeser 1977, Anthony 1979).

In 'tic douloureux', systemic administration of carbamazepine (Blom 1962) has succeeded alcohol blocks (Harris 1940) as the primary choice of treatment since many years (Campbell et al. 1966). About 70 % of the patients are said to report good or excellent analgesia initially (Rasmussen and Riishede 1970, Taylor et al. 1981). However, side-effects are frequent, often due to overdosage, and longterm follow-up studies have shown that only 25-35 % of the patients had excellent or good pain relief of more than five years duration with carbamazepine treatment only (Sundbärg 1974, Taylor et al. 1981). In the remainder, save for those few where systemically administered phenytoin is effective (cf.

Loeser 1977), surgical procedures are what remains. The early unselective techniques (see e.g. Peet and Schneider 1952) carried a significant risk of general as well as local complications (see Rasmussen 1965). The more selective techniques now used, such as controlled thermocoagulation of the trigeminal ganglion (Sweet and Wepsic 1974) and retrogasserian glycerol injection (Håkansson 1981) have fewer side-effects and can be repeated if necessary.

A different line of development has been based on the hypothesis that trigeminal neuralgia is a result of vascular compression of the trigeminal nerve root (Dandy 1934). Decompression by microsurgical procedures have been reported successful in 70-80 % of the patients treated (Apfelbaum 1977, Janetta 1980, van Louveren et al. 1982) even if the rate of significant compression found by the latter authors was low (46 %). However, all the surgical procedures involve potential hazards to the patients as well as a need for trained surgeons and in-patient facilities.

In 'atypical facial pain' (Rushton et al. 1959, Gregg 1978) whether with or without an identifiable organic cause, antiepileptic drugs are generally ineffective. Alcohol injections or surgery, even if temporarily relieving, may later result in a considerable worsening of the condition (Rasmussen 1965, Gregg and Grady 1975). Conventional analgesics may be useful when there is an organic cause, tricyclic antidepressants when there is not (Anthony 1979). The available therapeutic methods, however, leave many patients unaided and substantially handicapped by their chronic facial pain.

During the last decade treatment by conditioning stimulation of peripheral nerves has become increasingly used for acute and chronic pain conditions (Wall and Sweet 1967, Loeser et al. 1975, Long 1976). A long-term follow-up study of the effect of two types of transcutaneous electrical nerve stimulation (TNS) showed that after two years, 31 % of the patients still experienced useful analgesia from daily TNS treatment (Eriksson et al. 1979). Among these successfully treated patients with chronic pain were several with IFP, some of which had to use a newly developed TNS technique

(acupuncture-like TNS, Eriksson and Sjölund 1976) to get relief.

Apart from the need for alternative therapeutic methods among patients with IFP it seemed of great interest for the evaluation of the TNS techniques to test and follow a group of patients with chronic pain which was less varied as to type and location than in previous studies. We therefore initiated and here report the results of a prospective long-term follow-up study of 50 patients with intractable facial pain, treated with conventional or acupuncture-like TNS. The facial pain conditions treated can in fact be taken to represent mainly two types of pain, namely acute intermittent ('*tic douloureux*') and chronic continuous ('*atypical facial pain*').

MATERIAL

The study was performed on 50 consecutive patients with IFP, referred for consideration of surgery to the Department of Neurosurgery at Lund University Hospital.

Twenty-one patients had, when their history started, been classified as having '*tic douloureux*'. The diagnostic criteria were 1/ truly paroxysmal 2/ unilateral pain attacks, 3/ provokable by non-nociceptive facial stimuli, 4/ confined to the innervation area of one, two or three trigeminal branches with 5/ no sensory or other neurological deficit. There were 11 men and 10 women, the mean age was 65 (34-88) years and the median pain duration was 8 (2-18) years. All had initially experienced pain relief with carbamazepine. However, diminishing effectiveness of the drug or marked side-effects including allergic reactions had limited its usefulness or made use impossible. Repeated alcohol injections of one or several distal trigeminal branches had given temporary pain relief in 12 of 21 patients. Of these 12 patients, 7 had also been subjected to surgery, in most cases fractionated heating of

the Gasserian ganglion, but the procedures had only given short-term relief. As a result of repeated treatment with injections or surgery, three patients had over the years developed a more continuous aching pain and these and five more had sensory deficits.

Twenty-nine patients did not, when their history started, fulfill the above diagnostic criteria and will here be referred to as having 'atypical IFP'. In 18 of these patients the pain had followed on accidental or postoperative trauma (11 patients), cerebrovascular disease (5 patients) or zoster ophthalmicus (2 patients). In 11 patients no organic cause of the pain could be found. There were 17 men and 12 women, the mean age was 58 (23-84) years and their median pain duration 5 (1-30 years). All but one reported their pain to be almost constantly present, with exacerbations lasting for hours or days. It was described as deep, dull, aching or burning. Treatment with carbamazepine, conventional analgesics, antidepressants or sedatives, had not significantly relieved the pain and 17 patients had been subjected to repeated alcoholic injections and/or surgery, in some cases with partial or temporary effect.

METHODS

The symptomatic nature of treatment with TNS was explained and patient consent obtained. After the initial examination, including sensory testing of the head and neck area, stimulation treatment was tested in an open care unit according to the scheme described below and illustrated in Fig. 1. All patients were tested in an identical fashion. Later, instructions were individualized.

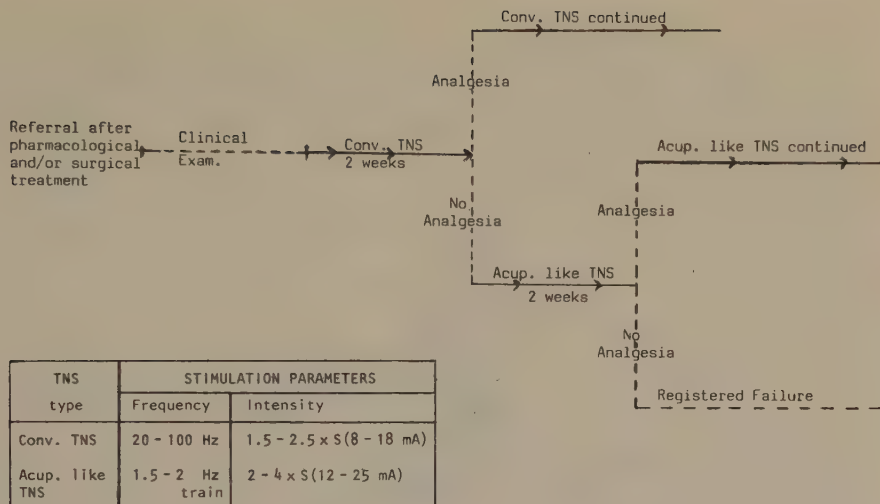


Figure 1. Scheme illustrating TNS treatment protocol. Conv = conventional, acup.like = acupuncture-like, S (sensory threshold) = the current at perception and threshold in mA.

First, conventional TNS was given with 100 Hz continuous stimulation at an intensity which gave strong paresthesiae without being painful (Fig. 2). One electrode was usually placed in front of the ear and the second electrode according to which trigeminal area was involved. Polarity was chosen according to patient preference. In some patients the most effective electrode position had to be assessed gradually.

Each patient was given a stimulator for home use and was instructed to apply TNS for a minimum of 30 minutes, three times daily. They were free to increase the number of stimulation sessions, if necessary. The patients with 'tic douloureux' were asked to be careful not to stimulate trigger points and recommended to use TNS at regular intervals, between attacks. They were told not to expect to be able to control on-going attacks and warned that stimulation treatment might actually worsen such an attack. If, after a two-week trial period at home, there was a verbal report of a generally lowered pain level and/or diminishing frequency or intensity of paroxysmal attacks, the patient was instructed to

carry on and to vary the stimulation frequency within the 20-100 Hz range in order to find the most comfortable frequency for pain relief. The patient was seen again, after another two weeks, and then after two months more.

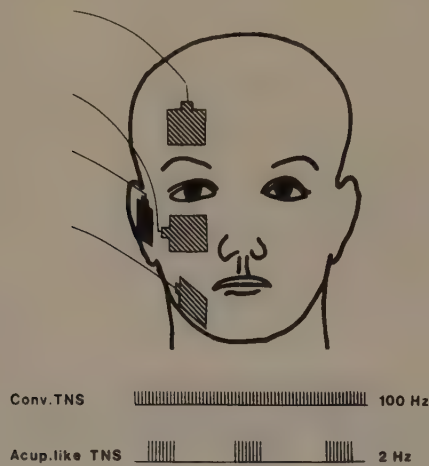


Figure 2. Top, electrode placements for acupuncture-like TNS. Anode (black) anterior to external meatus, cathode (active electrode, hatched) over center of pain. Bottom conv. TNS and acup.like TNS, stimulation patterns used as described in text. Abbreviations as in fig. 1.

If, after the first two-week trial period, there was no significant pain relief, the patient was given instructions how to use the stimulator for acupuncture-like TNS. The positive electrode was then placed in front of the ear and the negative electrode over the forehead, cheek or chin. The stimulator was set for 1.5-2 Hz train (7 pulses at 100 Hz) stimulation and the electrodes adjusted so that visible muscle contractions were produced in the area of pain (Fig. 2). If, after another two-week trial period at home, there was still no report of significant pain relief, the TNS trial was recorded as a failure. If stimulation treatment was reported to reduce the intensity and frequency of pain paroxysms, or produced useful pain relief in non-paroxysmal 'atypical IFP', the patient was instructed to carry on and was seen again two months later.

If the patients, when seen three months after their initial visit, reported useful pain relief and wished to continue TNS treatment, the outcome of therapy was recorded as successful. When patients continued to use small amounts of carbamazepine or other analgesic agents together with stimulation treatment, it was judged as moderately successful. All patients were seen with regular intervals for two years or until the treatment was terminated. When pain relief seemed stable or during periods of spontaneous remission patients were instructed to try to reduce the duration and frequency of the stimulation periods as much as possible.

The stimulator used is a portable constant current unit that delivers conventional or acupuncture-like TNS by monophasic square wave pulses of 0.2 ms duration at maximally 60 mA into a load of 2500 Ohm, (Cefar Medical Products, S-222 27 LUND, Sweden). The stimulation was given via standard square carbon rubber electrodes, usually = 6 cm², coated with conductive gel. Stimulation intensity (Fig. 1) was 1.5-2.5 times the perception threshold in conventional TNS (usually 8-18 mA) and 2-4 times the perception threshold in acupuncturelike TNS (usually 12-25 mA).

Statistical method

For evaluation of differences between groups the Chi-square test was used. If any of the calculated expected numbers for the four fields was ≤ 5 , Yates' correction was used.

RESULTS

From Fig. 3 it is seen that at three months of treatment 16/50 patients or 32 % experienced successful or moderately successful pain relief with conventional TNS only. Among the 34 patients who did not benefit from conventional TNS, acupuncture-like TNS proved to be satisfactory in another 13 patients. Thus, in all 29/50 patients or 58 % experienced pain relief from TNS. Twenty patients used stimulation only (success) and nine patients added small amounts of adjuvant pharmacotherapy (moderate success). Seven patients who had not been working for a long time because of their facial pain went back to work.

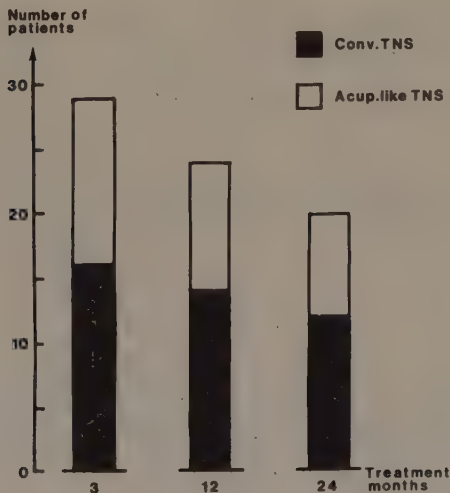


Figure 3. Treatment results at times indicated. Numbers of patients experiencing satisfactory pain relief given in relation to TNS technique used (key). Abbreviations as in fig. 1.

At twelve months, two patients had died from unrelated disease and one had a period of spontaneous remission and was not using the stimulator. Of the remaining 47 patients, 24 or 51 % were still using TNS, achieving satisfactory pain relief. At 24 months, three patients had a spontaneous remission of their pain and one more had died. Still not less than 20/44 or 45 % reported satisfactory

analgesia from TNS (Fig. 3).

Treatment results at three months were evaluated in relation to the TNS technique used, etiology and duration of the IFP condition, sex, main complaint of pain and results of sensory examination at the time when TNS treatment started (Table).

Table Outcome of TNS treatment in relation to patient material.

	<u>TNS success</u>	<u>TNS failure</u>
<u>Sex</u>		
Male	20(8)	8
Female	9 (5)	13
<u>Initial diagnosis</u>		
Typical trigeminal neuralgia	11(5)	10
Other forms of intractable facial pain		
Unknown etiology	4 (2)	7
Known etiology	14(6)	4
<u>Previous treatment</u>		
Pharmacological treatment only	13(5)	8
Alcoholic blocks or surgery	16(8)	13
<u>Duration of pain</u>		
≤ 6 years	19(7)	7
> 6 years	10(6)	14
<u>Main complaint</u>		
Pain paroxysms	8 (4)	11
Continuous pain	21(9)	10
<u>Cutaneous sensation</u>		
Normal	11(3)	8
Hypo- or dysesthesia	18(10)	13

Table. Figures denote number of patients in the various groups, figures within brackets denote patients preferring acupuncture-like TNS. For details, see text.

Of the 21 patients with 'tic douloureux', 11 were in the successful or moderately successful group. Five of these had to use acupuncture-like TNS (Table, numbers within brackets) to achieve satisfactory pain relief. Among the patients with 'atypical facial pain', 4 of 11 patients with unknown etiology experienced satisfactory relief, two of whom had to use acupuncture-like TNS. Similarly, among the 14/18 patients with known etiology of their pain, who were in the successfully or moderately successfully treated group, six patients employed acupuncture-like TNS. There was no significant difference in treatment success between patients with 'tic douloureux' (11/21) and atypical IFP (18/29). However, significantly ($0.025 < p < 0.05$) better results were obtained in patients who had 'atypical IFP' with a known organic cause as compared to all other patient groups (Table).

The median pain duration for all patients was six years. The TNS success rate was significantly ($0.025 < p < 0.05$) higher among patients with a pain history of less than six years than in the group with a longer history of facial pain (Fig. 4). The mean duration of pain was similar among men (7 years) and women (8 years) (cf. *infra*).

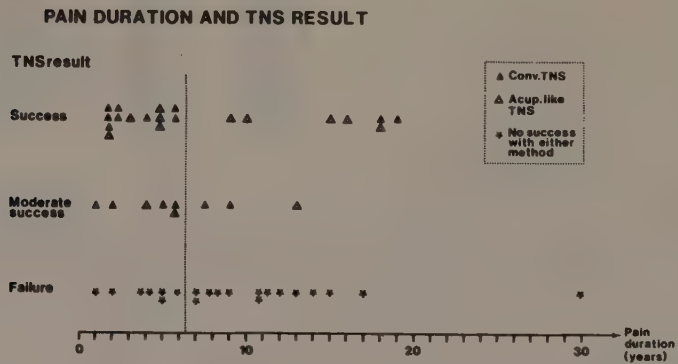


Figure 4. TNS results given in relation to pain duration and TNS technique used (key). Success and moderate success defined in text. Dotted line denotes median pain duration among these patients. Abbreviations as in fig. 1.

We found a significantly ($0.025 < p < 0.05$) higher number of men than of women in the successfully treated group. This is further illustrated in Fig. 5, where it can be seen that with 'atypical facial pain' of unknown and known origins, the representation of men and women in relation to success or failure is proportional to their total numbers in the diagnostic groups. On the other hand, among patients with 'tic douloureux', the representation of men in the successful group was higher than expected.

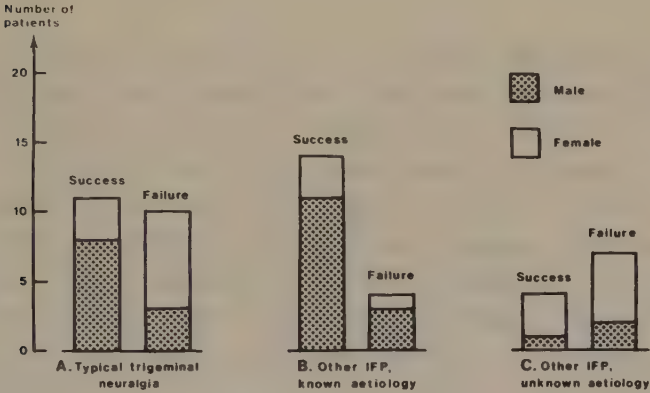


Figure 5. TNS results in relation to diagnosis of intractable facial pain (IFP) and patient sex.

There was a non-significant tendency for truly paroxysmal facial pain to be more resistant to stimulation treatment (11/19) than pain of the more continuous type (10/31, Table). In an earlier report (Eriksson et al., 1979), acupuncture-like TNS was noted to be of special value when destructive surgery had been performed with resulting cutaneous hypesthesia or dysesthesia within the area of pain. In the present group of patients with facial pain, there was no significant difference between those with normal sensitivity (3/11) and those with hyp-/dysesthesia (10/18) as regards method of stimulation.

Side-effects were few. Four patients with typical trigeminal neuralgia reported intensified pain if TNS was used during the actual pain paroxysms. Four patients had marked skin reactions which could be handled by change of electrodes and tapes. Side-effects did not cause termination of treatment in any of these patients.

DISCUSSION

The present study has confirmed our initial observations (Eriksson et al. 1979) that TNS may be a worthwhile choice of therapy in intractable facial pain. Thus, among the present patients with 'tic douloureux', often of considerable duration, about half of the patients found TNS therapy to give satisfactory pain relief and among those with 'atypical facial pain', two thirds did so after three months of treatment. Still after two years, 45 % of the 44 patients remaining in the study used TNS regularly and experienced satisfactory relief. No serious side-effects were seen.

Considering the severity of the conditions in these patients, all judged to be treatment failures as regards conservative treatment, the results show that TNS therapy may well be a relevant alternative to surgical procedures. This may be so for 'tic douloureux' especially in the elderly, where surgical risks are more significant (Apfelbaum 1977, Janetta 1980), and for the group of patients with 'atypical facial pain' as a whole, where surgical results are not encouraging (Rasmussen 1965, Gregg 1978).

Interestingly, the newly introduced technique of acupuncture-like TNS (Eriksson and Sjölund 1976) seems to have improved the results considerably as compared to the use of conventional TNS (Wall and Sweet 1967) only. This may well explain that our results with IFP are superior to those reported by others (Thoden and Krainik 1974, Gregg 1978, cf however, Ihalainen and Perkki 1978).

The treatment success seen after two years in this group (45 %) is higher than that reported by us in a previous study of patients consecutively referred for chronic pain to the same pain treatment unit (Eriksson et al. 1979). One possible explanation for this is the relative ease with which coarse nerve bundles in the facial region are stimulated as compared to many other body areas. Another explanation may be that the pain conditions were well defined and neurogenic (cf. Sindou and Keravel 1980) and a third that psychogenic factors were less dominating in this group (cf. Nielzén et al. 1982).

Among factors predictive for the outcome of TNS, a short duration of the pain condition was positive in relation to results. So was a known precipitating cause among the patients with 'atypical facial pain'. However, the tendency for 'atypical facial pain' to be more amenable to TNS therapy than 'tic douloureux' was not significant. Interestingly, men with IFP, notably those with 'tic douloureux', showed better treatment results than women. This might indicate that the men in this sample adjusted better to the occasionally unpleasant stimulation, which also, due to the facial electrodes, could be considered a social handicap, even if used only 30-90 min. a day. Moreover, psychogenic factors may have been more important among the women (cf. Speculand et al. 1981, Nielzén et al. 1982).

As regards the possible mechanisms of action of conventional and acupuncture-like TNS it is interesting that both techniques seem to relieve pain conditions of acute intermittent ('tic douloureux') as well as of chronic continuous ('atypical facial pain') character. This appears to hold for pains of presumed peripheral as well as of presumed central origin. Thus, successfully treated 'atypical facial pain' was in some instances due to peripheral lesions (zoster neuritis, trauma), in other to cerebrovascular disease. 'Tic douloureux' has been ascribed to peripheral (nerve root compression, Dandy 1934, segmental demyelination, Kerr 1967, exaggerated dorsal root reflexes, Calvin et al. 1977) as well as to central causes (Kugelberg and Lindblom 1959). Taken together,

these observations favour a central mechanism of action for TNS. This is in agreement with the observation that analgesia from acupuncture-like TNS is usually naloxone-reversible (Sjölund and Eriksson 1979) indicating an opioid link. However, analgesia from conventional TNS cannot be reversed by naloxone (Sjölund and Eriksson 1979). On the other hand, both techniques change sensory thresholds of healthy subjects on both sides after unilateral stimulation, supporting the concept of a central mechanism (Eriksson et al. 1980).

Acknowledgements

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THE INFLUENCE OF NALOXONE ON ANALGESIA PRODUCED BY PERIPHERAL CONDITIONING STIMULATION

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SUMMARY

Conditioning electrical stimulation of peripheral nerves is presently routinely employed for alleviation of chronic pain in humans. Most commonly, high frequency stimulation of probably mainly coarse myelinated afferents from the skin is used as proposed in the gate theory of Melzack and Wall²⁵. However, only a limited number of patients benefit from such stimulation. To improve the results of such treatment we have developed a kind of acupuncture-like electrical stimulation where mixed nerves are stimulated with short trains of stimuli given at a slow repetition rate via surface electrodes to elicit muscle contractions. The compiled results of conditioning stimulation for analgesia were then markedly improved.

To see whether the analgesia experienced by the chronic pain patients is mediated via links utilizing endorphins, the opiate antagonist naloxone was administered to these patients under double-blind conditions, saline being used as a placebo. We then found that 6 out of 10 patients receiving acupuncture-like stimulation but none out of 10 patients receiving high frequency stimulation of skin nerves, reported an inhibition of the stimulation-produced analgesia by naloxone. This indicates that the analgesia produced by acupuncture-like stimulation is mediated via mechanisms utilizing endorphins whereas the analgesia produced from high frequency stimulation of coarse cutaneous afferents is mediated via some other mechanism.

INTRODUCTION

In recent years transcutaneous electrical stimulation of peripheral nerves (transcutaneous nerve stimulation; TNS) and direct stimulation of the dorsal columns of the spinal cord via implanted electrodes (dorsal column stimulation; DCS) have become routine methods of alleviating chronic pain in humans. This therapy was initiated from the gate theory of Melzack and Wall²⁵ postulating that activity in coarse

primary afferent fibres preferentially mediating touch would lead to presynaptic inhibition in the dorsal horn of the activity in thin afferent fibres, mediating pain. The experimental evidence underlying this theory (e.g. ref. 26) has been criticized and shown to be partly wrong (see ref. 30). However, many reports have been published on the clinically useful analgesia produced by high frequency electrical stimulation of peripheral nerves at an intensity sufficient to stimulate mainly coarse myelinated fibres^{21,22,27,31,37}. On the other hand, in the long run only 10–40% of the patients experience sufficient pain relief from such conditioning stimulation^{21,22}.

We have therefore developed a new kind of peripheral conditioning stimulation for the induction of analgesia, where experiences from the Chinese electro-acupuncture have been utilized. With electro-acupuncture, instead of twirling the inserted needles, high intensity electrical pulses are given via the needles, usually at a low frequency of about 1–2/sec^{3,20}. Western observers visiting China have described that surgical interventions may take place with acupuncture or electro-acupuncture as the only analgesic procedure^{6,20}. A rise in tooth pain threshold in healthy volunteers has also been found with acupuncture treatment^{3,9,18}. To achieve the rise in tooth pain threshold, Andersson and Holmgren had to use stimulation strengths of 5–8 times perception threshold⁵ that elicited strong muscle contractions in related myotomes. These workers also found that the rise in pain threshold was achieved as readily with stimulation via surface electrodes as with stimulation via needles. Unfortunately, this low frequency, high intensity stimulation was not effective in chronic pain patients, partly due to the difficulties of the patient in tolerating the high stimulation intensity⁴ (cf. also ref. 15). By substituting a short train of pulses for the single pulse, we could decrease the stimulation intensity to tolerable levels (3–5 times perception threshold); maintaining the seemingly necessary forceful muscle contractions¹². With this acupuncture-like stimulation analgesia was produced in many patients with chronic pain resistant to conventional TNS^{12,13}.

How do the two kinds of peripheral conditioning stimulation produce analgesia? The specific narcotic antagonist naloxone¹⁹ has been reported to counteract the rise in tooth pain threshold seen after classical needle acupuncture^{23,24}, indicating that a release of endorphins¹⁶ might be responsible for the effect. We therefore considered it important to investigate the influence of naloxone on the analgesia produced by either type of stimulation in humans with chronic pain. A preliminary report has been published³².

METHODS

Twenty volunteer patients with chronic pain of long duration participated in the present study. Ten of these patients were treated with conventional TNS (e.g. ref. 22) of monophasic square pulses (duration 0.2 msec) given at a high frequency (50–100 Hz) and a low intensity (2–3 times perception threshold). Another 10 patients were treated with acupuncture-like TNS, where short trains of the same kind of monophasic pulses (70 msec; 100 Hz internal frequency) were given at a low frequency (2 Hz) and at a strength of 3–5 times perception threshold¹². The stimuli were given via carbon

rubber electrodes sized 14 sq. cm coated with conducting gel and placed over nerve branches innervating the painful segment (dermatome or myotome). All the patients had received their treatment with portable constant current stimulators (CEFAR S III, AB CEFAR, Sweden) for at least 3 months, usually 10–30 min one to four times daily. The degree of pain relief was 50–100%, as scored on a visual analogue scale²⁸. Naloxone hydrochloride (Nalone, Endo) was given i.v. in a 0.4 mg/ml solution. As a rule, two test injections of 0.8–1.6 mg were first administered while experiencing analgesia from stimulation. If the pain returned within 10 min, a double-blind experiment was always performed with a series of 4–8 i.v. injections at 30 min intervals. In some patients, however, the double-blind procedure was performed directly. Sterile saline of the same volumes was used as placebo. Ten minutes after each injection the pain intensity was scored by the patient on a visual analogue scale. Changes in pain intensity of less than 10% of the scale length were considered uncertain (cf. Fig. 2).

RESULTS

Typical results from a patient receiving acupuncture-like low frequency TNS are shown in Fig. 1. In A, the full visual analogue scale length with its verbal instructions is shown. In B and C, the results from two double-blind test sessions are given and it can be seen that the complete pain relief induced in this patient was markedly reversed by the administration of naloxone. With the first injection in B, the analgesia was even fully abolished, i.e. the patient's pain returned to the intensity before stimulation. The results from all the 10 patients receiving acupuncture-like TNS can be seen in Fig. 2A. Here the patients' reactions to test doses of naloxone are given as open circles and

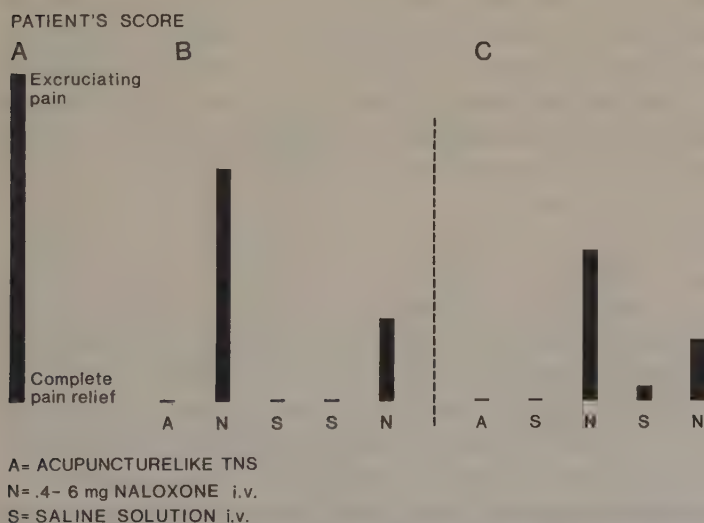


Fig. 1. Reaction to naloxone after receiving acupuncture-like TNS. A: visual analogue scale used by the patient to score pain intensity²⁸, B and C: pain scores given as scale lengths in test sessions performed under double-blind conditions with one patient at two different occasions. Abbreviations according to key.

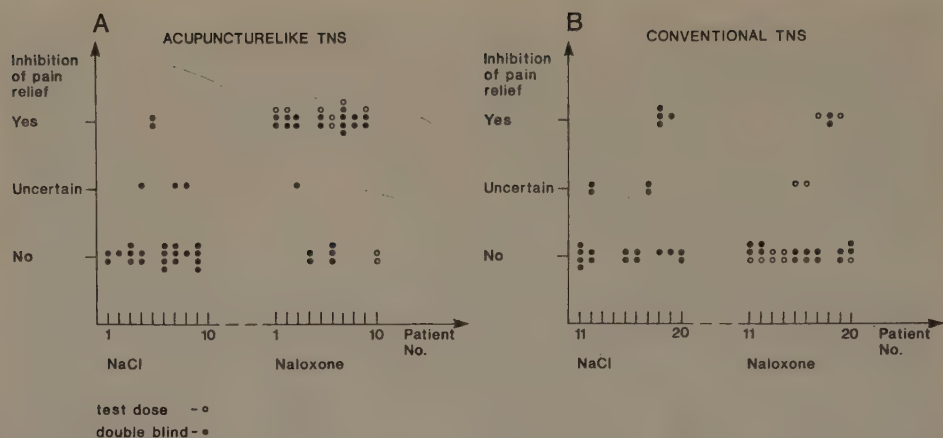


Fig. 2. Influence of naloxone on analgesia from acupuncture-like (A) and from conventional (B) TNS. Patients 1–10 received acupuncture-like TNS, patients 11–20 received conventional TNS. Reactions to saline and naloxone given separately for each patient. Inhibition of pain relief scored as described in Methods. Symbols, see key.

the reactions to saline or naloxone administered in double-blind fashion are illustrated as filled circles. The reactions to saline are shown in the left part of the diagram and those to naloxone are shown in the right part of the diagram. It can then be seen that patients 1, 2, 3, 7, 8 and 9 consistently experienced inhibition of pain relief from naloxone but not from saline. Patient 5 indicated inhibition of pain relief both from naloxone and saline injections. Patients 4, 6 and 10, on the other hand, did not experience any change in the pain relief induced by acupuncture-like TNS from naloxone or saline administration.

In Fig. 2B the corresponding results are shown for the patients receiving conventional high frequency TNS. None of these patients systematically experienced any inhibition of pain relief from naloxone. One patient, no. 18, reported inhibition of pain relief to 5 out of 6 injections, containing either saline or naloxone. All patients in both series that reported no change of pain intensity received at least two injections of 1.6 mg naloxone i.v. before the observations were considered valid.

DISCUSSION

The pure opiate antagonist naloxone has proved to be of great value in elucidating the pharmacological actions of opiates (see ref. 34). But for a long time few if any biological effects were reported when the drug was administered to healthy volunteers^{11,19}. However, using signal detection theory, Buchsbaum et al.⁷ found that pain-insensitive individuals reacted to naloxone with an increased pain sensitivity. Similarly, Frederickson et al.¹⁴ found that naloxone markedly reduced a spontaneous diurnal variation in the pain responsivity of mice. Furthermore, analgesia produced by stimulation of certain midbrain structures including the periaqueductal gray matter both in animals² and man¹ was reversed or partly reversed by naloxone. Likewise, Mayer et al.^{23,24} found that this agent reduced the tooth pain threshold increase seen

in healthy volunteers after classical needle acupuncture. On the other hand, Goldstein and Hilgard¹⁷ did not find any effect of naloxone upon the analgesia induced by hypnosis.

The present observations on patients in chronic pain treated with peripheral conditioning stimulation show that 6 out of the 10 patients receiving acupuncture-like TNS consistently experienced inhibition of the induced pain relief from intravenous injections of naloxone, whereas the 10 patients receiving conventional TNS did not. The obvious interpretation is that the analgesia from acupuncture-like TNS is mediated via links utilizing endorphins while conventional TNS induces analgesia via some other mechanism. Considering the acupuncture-like stimulation, our findings are in agreement with those of Mayer et al.^{23,24} and with the abolition by naloxone of the increased latency to squeak in mice after 'acupuncture'²⁹. Similarly, Chapman and Benedetti⁸ found that the tooth pain threshold increase from low frequency, high intensity single pulse stimulation in healthy volunteers was partially antagonized by naloxone. On the other hand, although reporting that the 'analgesia' in rats from conventional TNS was antagonized by naloxone in a tail immersion test³⁸, Woolf et al. found no reversal of the relief of acute pain in humans by the same kind of high frequency stimulation³⁹.

There are now several indications that conventional TNS on one hand and acupuncture, electro-acupuncture or acupuncture-like TNS on the other, have different mechanisms of action. Using selective peripheral nerve blockades, Chiang et al.¹⁰ found that the input from nerves innervating deep structures in areas stimulated in acupuncture was necessary for the analgesic effect. To achieve the rise in tooth pain threshold, Andersson and coworkers^{3,4} found it necessary to use a stimulation intensity eliciting strong muscle contractions. To induce analgesia from conventional TNS, direct stimulation of superficial nerve branches within a painful skin area is often sufficient^{21,22,37}. Furthermore, whereas a slowly rising, lasting increase in pain threshold is seen with acupuncture or electro-acupuncture^{3,9,35}, only a transient increase of the pain threshold has been seen with conventional TNS^{5,18}. Interestingly the induction time for analgesia in acupuncture-like TNS is 20–30 min, which is significantly longer than that for conventional TNS, where many patients report instant analgesia¹². The long induction time might imply that a substance (endorphin?) is slowly liberated or secreted to achieve inhibition in the pain pathways. Measurements of two endorphin fractions in human cerebrospinal fluid³⁶ indicate that in chronic pain the content of one of the fractions is lowered. After acupuncture-like TNS the content of this endorphin fraction (I) increases to normal or supernormal values in the cerebrospinal fluid when sampled near the point of stimulation³³. In pilot experiments, such increase of the cerebrospinal fluid endorphin content was not seen with conventional TNS (Terenius, pers. commun.).

To conclude, the present study indicates that the CNS possesses at least two systems for control of the transmission in the pain pathways that can be influenced independently from the periphery. These systems can effectively combat chronic pain in humans, but to define their role under physiological conditions remains for further studies.

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THERMAL SENSITIVITY IN HEALTHY SUBJECTS IS DECREASED BY A
CENTRAL MECHANISM AFTER TNS

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SUMMARY

Using the thermal sense as a model for nociception, the effects of conventional and acupuncture-like transcutaneous nerve stimulation (TNS) was tested on thresholds for warm and cold sensation in 8 healthy subjects. Photic stimulation did not change the thermically neutral zone (the warm-cold difference limen) from that seen under baseline conditions. However, the thermal difference limen usually increased with both types of TNS. The effect was ipsi- as well as contralateral, implying that a central inhibitory mechanism is activated by conventional and acupuncture-like TNS.

INTRODUCTION

Conditioning stimulation of peripheral nerves for pain relief, so called transcutaneous nerve stimulation (TNS) has been used in patients with chronic pain for more than a decade (see e.g. Ray and Maurer 1975, Sjölund and Eriksson 1980). Still, however, its mechanism of action is not known.

The TNS technique was introduced as a consequence of the gate theory (Melzack and Wall 1965) by Wall and Sweet (1967). They used weak electrical stimulation of nerve bundles, eliciting non-painful paraesthesiae in the region treated. The pain relief elicited was mainly ascribed to an increased presynaptic inhibition in thin nociceptive afferents via spinal interneurons. Criticism was, however, risen both against the experimental background of the theory (e.g. Schmidt 1972) and the theory as such (Nathan 1976). Campbell and Taub (1973) maintained that the analgesic effect seen after TNS could well be explained by a fatigue phenomenon in nociceptive afferent axons, stimulated by the TNS technique. This appeared to be supported by some experimental studies in animals (Ignelzi and Nyquist 1976, 1979).

Since peripheral (Torebjörk 1974, Darian-Smith and Johnson 1977, LaMotte and Campbell 1978, Adriaensen et al. 1980) as well as central (see Webster 1977) pathways mediating thermal and nociceptive information seem to be similarly organized, the thermal sense was used as a model for pain in the present study. Furthermore, thermal sensory thresholds (warm-cold difference limen) can be determined with high reproducibility by a recently devised technique (Fruhstorfer et al. 1976). To get an indication if TNS really induces central changes in man we decided to examine thermal thresholds within and outside the innervation area of a nerve bundle stimulated.

We studied both the TNS technique already described (here denoted conventional TNS) and a recently developed new TNS technique (Eriksson and Sjölund 1976). The latter technique is used mainly when pain relief is not achieved from conventional TNS (Eriksson et al. 1979) and probably utilizes an endorphinergic link (Sjölund et al. 1977, Sjölund and Eriksson 1979).

MATERIAL

Eight healthy subjects, seven female and one male, age 22-28 years. The spontaneous skin temperature in the thenar regions was controlled before the test and was $\geq 30^{\circ}$ C in all subjects.

METHODS

Thermal sensitivity

Thermal sensitivity was tested with a thermal stimulator patterned after the Marstock stimulator of Fruhstorfer et al. (1976). The device consists of a ceramic plate (30 x 30 mm), mounted on a Peltier element, with a surface embedded thermistor. The ceramic surface can be warmed or cooled at a rate of 1.0-1.5° C/sec, the direction of temperature change being reversed by pressing a hand-held button (Fig.).

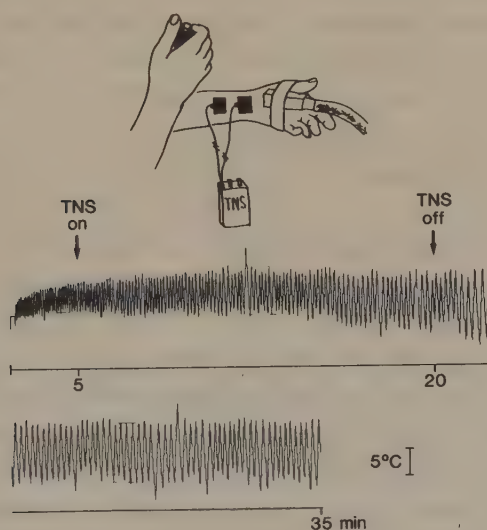


Figure: Top: Schematic drawing of the experimental situation. Thermal stimulator attached over thenar region, TNS electrodes over median nerve. Bottom: Continuous recording over 35 minutes of warm-cold difference limen (up=warm, down=cold) during one experiment as described in the text (subject 5, conventional TNS, ipsilaterally). Thin lines indicate the measurements made.

The ceramic plate was applied to the thenar region (Fig., top) and the subject instructed to press the button at the first warm sensation, usually in the 34-38° C range, when the temperature was increasing, or at the first cold sensation, usually in the 31-35° C range, as the temperature decreased. The temperature reversal button was held in the other hand. The skin surface

temperature was monitored on a calibrated chart recorder, and the temperature difference between warm and cold sensation was measured in °C and expressed as the "warm-cold difference limen".

The effect of non-painful transcutaneous nerve stimulation on sensitivity to threshold temperature was tested for conventional and acupuncture-like TNS, ipsi- and contralaterally. The electrodes were placed over the median nerve at the wrist and after five minutes recording under baseline conditions, TNS was given for 15 minutes (conventional TNS: 80 Hz, at an intensity 2-3 times the sensory threshold producing strong paraesthesiae; acupuncture-like TNS: 2 Hz, at an intensity 3-5 times the sensory threshold, producing strong visible muscle contractions). After stimulation was terminated, the temperature threshold recording was continued for another 15 minutes.

The total recording time of each test was 35 minutes, in pilot studies found to be the maximum tolerated by the subjects without significant changes in the level of wakefulness. For each subject two 35 minute control recordings were made, one during baseline conditions and one during five minutes of baseline conditions, five minutes of photic stimulation and another 25 minutes rest.

The six tests (two control recordings, two recordings ipsilateral and two contralateral to the conditioning stimulation) were performed in a random order for each subject. The instructions stressed that the temperature-reversal button should be pressed when a cold or warm sensation was actually felt - not anticipated - and the laboratory surroundings were kept quiet, isothermic and identical. The recordings were made by one of the authors, the measurements of the warm-cold difference limen records by another who was unaware of the particular test performed.

RESULTS

A typical experiment is illustrated in the figure (bottom). After the recording of baseline thresholds (up=warm, down=cold), stimulation was started with electrodes placed over the median nerve. The thermal sensitivity of the thenar region was continuously monitored during stimulation (15 min) and for 15 min thereafter. The warm-cold difference limen (Fruhstorfer et al. 1976) in this experiment can be seen to increase with stimulation, indicating a decreased thermal sensitivity. This occurred both for sensitivity to warmth (up) and to cold (down). A slight further decrease of thermal sensitivity was seen in the poststimulatory period in this and several other experiments.

In the Table, the warm-cold difference limen ($^{\circ}\text{C}$) for each subject is given repeatedly during the various test sessions. Each value is the geometrical average over two minutes. Values are given at 4-5 minutes (baseline), after 7-8 minutes of TNS (TNS), after 2-3 minutes of photic stimulation (Photic stimul.) or in poststimulatory or rest periods at times indicated. As can be seen from the lower part of the Table (CONTROLS) the limen did at no occasion deviate more than 50 % from baseline value during rest or photic stimulation. Therefore, only changes in thermal limen greater than 50 % were evaluated as positive (+ in Table) with respect to TNS.

Using this technique of evaluation, it turned out that in six out of eight subjects, the warm-cold difference limen increased more than 50 % when conventional or acupuncture-like TNS was applied ipsilaterally. Interestingly, the same changes were also seen contralaterally to the stimulation, in five out of six subjects with both types of stimulation. In addition one subject in each group showed a contralateral change only. In half of the subjects after-effects of varying degrees were seen with one or both types of TNS. On the other hand, subject S3 seemed unsensitive to TNS in that no changes greater than those under control conditions were seen.

WARM - COLD DIFFERENCE LIMEN IN °C

CONVENTIONAL TNS	S1	S2	S3	S4	S5	S6	S7	S8
Baseline	2.0	1.8	4.0	4.5	5.0	1.5	2.0	3.0
TNS, ipsilat.	2.5	3.5	6.0	9.5	9.0	5.0	5.0	4.5
Poststimul. 2 min.	3.2	2.5	5.5	5.0	9.0	2.5	4.5	3.5
Poststimul. 8 min.	3.2	2.2	5.5	5.0	10.0	2.0	5.0	4.0
Poststimul. 15 min.	4.0	2.0	5.5	5.0	10.5	2.0	6.0	4.0
Evaluation	+	+	-	+	+	+	+	-
Baseline	1.0	2.0	3.0	5.0	6.5	1.5	2.0	2.5
TNS, contralat.	2.5	4.5	4.0	6.5	10.5	3.0	4.5	5.0
Poststimul. 2 min.	1.6	5.5	4.0	5.5	9.5	3.0	2.0	4.5
Poststimul. 8 min.	1.6	5.0	3.5	5.0	9.5	2.8	2.0	4.5
Poststimul. 15 min.	1.0	4.0	3.5	5.0	9.5	2.5	2.0	4.5
Evaluation	+	+	-	-	+	+	+	+
ACUPUNCTURE-LIKE TNS								
Baseline	1.7	2.0	3.5	4.0	7.0	3.0	3.5	3.5
TNS, ipsilat.	3.0	5.0	5.0	7.0	24.0	3.5	7.0	6.0
Poststimul. 2 min.	1.5	4.5	5.0	6.0	17.0	3.5	5.5	6.0
Poststimul. 8 min.	1.5	3.0	4.8	5.7	12.5	3.5	5.5	5.0
Poststimul. 15 min.	1.5	3.0	4.5	5.5	11.0	3.0	6.5	6.0
Evaluation	+	+	-	+	+	-	+	+
Baseline	1.0	2.5	3.5	3.0	5.0	1.5	2.0	3.0
TNS, contralat.	1.5	5.5	3.5	6.5	9.0	6.8	4.5	5.5
Poststimul. 2 min.	1.4	5.5	3.0	5.0	8.0	6.5	3.0	4.5
Poststimul. 8 min.	1.0	5.3	3.0	5.0	8.0	5.5	2.7	4.5
Poststimul. 15 min.	1.0	3.0	3.0	5.0	8.0	4.0	2.5	4.5
Evaluation	-	+	-	+	+	+	+	+
CONTROLS								
Baseline	1.5	1.9	3.5	1.5	4.0	1.8	3.0	2.0
Photic stim.	1.5	2.0	3.5	1.5	4.5	1.9	4.5	2.5
Poststimul. 2 min.	1.5	1.9	3.0	1.5	4.5	1.8	4.5	2.0
Poststimul. 8 min.	1.5	2.0	3.0	1.5	5.0	1.8	4.0	2.0
Poststimul. 15 min.	1.5	2.0	3.0	1.5	5.0	1.9	4.0	2.0
Evaluation	-	-	-	-	-	-	-	-
Baseline	2.0	2.2	5.5	3.5	7.0	1.8	3.5	5.0
Rest 10 min.	2.0	2.3	5.5	3.8	6.0	1.8	4.8	4.0
Rest 20 min.	2.0	2.3	6.5	4.5	6.0	1.8	4.0	4.0
Rest 30 min.	2.0	1.9	6.5	4.2	7.8	1.8	3.5	4.0
Evaluation	-	-	-	-	-	-	-	-

Table. Warm-cold difference limen values of each subject as obtained in the six tests. For details, see text.

Since warm sensation is probably transmitted mainly via C-fibres and cold sensation via A-delta fibres (Darian-Smith and Johnson 1977) a systematic change in the threshold of either of these qualities would have been particularly interesting. However, this was not observed.

DISCUSSION

In the present study, utilizing the thermal sense as a model for the transmission of nociceptive stimuli, it was found that six out of eight subjects displayed a decreased thermal sensitivity during and after TNS within the innervation area of the nerve bundles stimulated. Similar results were seen with both TNS techniques and as concerns conventional TNS this is in agreement with changes in measures of experimental pain observed by Higgins et al. (1971), Satran and Goldstein (1973) and Procacci et al. (1977). On the other hand, some workers (Campbell and Taub 1973, Nathan and Rudge 1974, Andersson and Holmgren 1976, 1978, Woolf 1979) found no or limited changes in the perception of experimental pain after TNS at non-noxious intensity (cf. also Lindblom and Meyerson 1975). With acupuncture and acupuncture-like stimulation techniques there is more agreement as regards elevation of experimental pain thresholds (Andersson et al. 1973, Andersson and Holmgren 1976, 1978, Chapman et al. 1976, Mayer et al. 1977).

The variations in poststimulatory effects seen as well as the fact that one subject (S3) was uninfluenced by the stimulation agrees well with the individual variations seen with the relief of chronic pain by these techniques (e.g. Eriksson et al. 1979). Furthermore, the unchanged thermal limen during and after photic stimulation suggests that the increase seen during TNS was not merely due to arousal or distraction.

More importantly, a decreased thermal sensitivity was seen contralaterally to the stimulation in six of the eight subjects when they received conventional as well as acupuncture-like TNS in the present study. This change would have to occur via a central mechanism and is a strong indication that TNS can induce marked (and long-lasting) alterations in the processing of sensory stimuli by the central nervous system.

Even if a peripheral mechanism of action of TNS (Campbell and Taub 1973, Ignelzi and Nyquist 1976, 1979) cannot be excluded by the present observations, they rather support a central mechanism of action. Furthermore, at least for acupuncture-like TNS, pharmacological studies suggest an opioid, i.e. central, link (Sjölund et al. 1977, Sjölund and Eriksson 1979). In addition, a peripheral fatigue phenomenon would imply stimulation of nociceptive afferents but TNS as used by us and others is not painful (e.g. Wall and Sweet 1967, Ray and Maurer 1975, Eriksson et al. 1979).

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Psychiatric Factors Influencing the Treatment of Pain with Peripheral Conditioning Stimulation

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Summary

Sixty-six patients treated with transcutaneous nerve stimulation (TNS) for pain symptoms were studied with respect to the incidence of different psychiatric factors and physical disorders in relation to success or failure of the treatment. In a blind screening procedure, mental illness and pathological personality traits were negative in relation to treatment success, while a state of reactive decompensation was not. Patients without any relevant physical cause of their pain were generally treatment failures and they had an excess of pathological personality traits, mostly of a hysterical nature.

Introduction

Peripheral conditioning stimulation of various kinds (e.g. transcutaneous nerve stimulation or TNS; acupuncture) has recently become widely used to alleviate chronic pain [see 4,5,9]. In our own work with peripheral conditioning stimulation it soon became apparent that patients complaining of chronic pain without, however, having any objective signs of physical disorders often did not respond to treatment. It is well known that the experience of pain is dependent on psychological factors. Several workers have pointed out that chronic pain may even originate from mental disturbances [3,6,12], both in neuroses, psychoses and in situational problems [15]. It has also been found that patients without obvious physical disorders do not differ in their subjective pain experiences from patients with such disorders [2].

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However, there are now biochemical findings indicating fundamental differences between pain states with and without physical cause. On measuring the endorphin content of the cerebrospinal fluid in patients with pain, it turned out that only those with pain of organic origin had an abnormally low endorphin content as compared to a control group. On the other hand, patients with pain due to psychological factors had a normal or even increased endorphin content [1,11,13].

In a previous follow-up study of TNS treatment we found a tendency for patients with pain due to mental factors to be overrepresented among those not responding to TNS [4]. We therefore considered it important to carry out a blind study, where groups of patients with and without analgesia from TNS were screened and compared regarding certain psychiatric variables. Indeed, marked differences were found between the groups indicating that some of the variables may serve as predictors for the outcome of TNS treatment.

Methods

Among patients with chronic pain referred to a tertiary level multidisciplinary pain unit (from a general practitioner via a specialist to a neurosurgical department) and treated with TNS according to the schedule reported in a previous paper [4], 46 patients reporting no analgesia were chosen from consecutively submitted patients. Twenty patients were then chosen from patients reporting satisfactory pain relief from TNS to form a control group, with respect to possible equation for sex, age and duration of pain. The patients were intermingled and subjected to a blind psychiatric consultation (1 h) the psychiatrist (S.N.) not knowing the outcome of TNS treatment. Questions related to pain treatment (including TNS) were avoided in this interview.

From the psychiatric evaluation the patient was put in either of 5 categories: mental illness (I), pathological personality traits (II), situational problems (III), state of reactive mental decompensation (IV) or no psychopathological signs (V).

By *mental illness* was meant depressive states with somatic manifestations (psychomotor retardation, sleep disturbances, anxiety with accent in the mornings) or psychosis whether it be of schizophrenic nature with disturbed perception, hallucinations or disorders of thought or of an organic or psychogenic nature with confusional or delusional traits.

Pathological personality traits were considered at hand when patients showed clear signs of at least one of the following items: evasion, denial, projection, repression to an incapacitating and unrealistic level, severe rigidity or affective instability. (These symptoms are frequent in clinical groups with diagnoses like hysteric neurosis and paranoid or immature personality.)

Situational problems were considered evident when one of the following events had been prominent: loss of object, loss of autonomy, sexual problems, problems in personal relationships, occupational or economical problems, immigrant problems or substance/alcohol abuse.

By *state of reactive mental decompensation* was meant one of the following

conditions: depressive, anxious or neurasthenic reactions. In some neurotic patients a stress-induced accentuation of their specific symptoms such as hysteric or phobic symptoms was interpreted as a sign of decompensation.

The statistical method used was that of χ^2 test [10].

Results

The distribution of patients within the various categories as related to the experience of satisfactory analgesia with TNS treatment is shown in Table I. The occurrence of psychiatric symptoms is high in both groups but the symptom profile differs significantly between them. Thus, the incidence of mental illness (I) and of pathological personality traits (II) was higher among the patients reporting no relief from TNS than among those experiencing pain relief. On the other hand, a minor mental disturbance (reactive decompensation, IV), was more common among the latter patients. Nine of the 46 patients who did not experience satisfactory pain relief were grouped in category I (mental illness), 3 patients of whom had depressions, another 3 had organic psychosyndromes, one had a paranoid psychosis and two suffered from senile cerebral lesions. There was no difference between the groups as regards situational problems (III). Among the patients rated in category IV, about equal shares of cases with anxiety, accentuated neuroticism, neurasthenia and reactive depression were encountered.

In order to evaluate whether the presence of a relevant physical cause (RPC) of the pain influenced the outcome of the treatment, the patients were further classified with respect to this variable as evident from patients' records and a neurological examination. It then appeared (Table II) that 19 of the 20 successful patients had an RPC, whereas only 24 of the 46 patients experiencing no or insufficient pain relief had an RPC, a highly significant difference ($P < 0.001$ in χ^2 test). Interestingly, when subdividing the patients into the 5 categories, the RPC incidence in the more severe categories I and II was significantly higher among the unsuccessful patients. On the other hand, patients with minor mental disturbance (IV) were more common

TABLE I

PSYCHIATRIC CATEGORIZATION IN RELATION TO SUCCESSFUL AND UNSUCCESSFUL PAIN ALLEVIATION FROM TNS IN 66 PATIENTS WITH CHRONIC PAIN

n, number of patients; n.s., no significance (χ^2 test).

Category	Success (n = 20)	No success (n = 46)	χ^2 test
I. Mental illness	0	9	$P < 0.05$
II. Pathological personality	2	19	$P < 0.025$
III. Situational problems	5	11	n.s.
IV. Reactive decompensation	9	4	$P < 0.001$
V. No psychopathological signs	4	3	n.s.

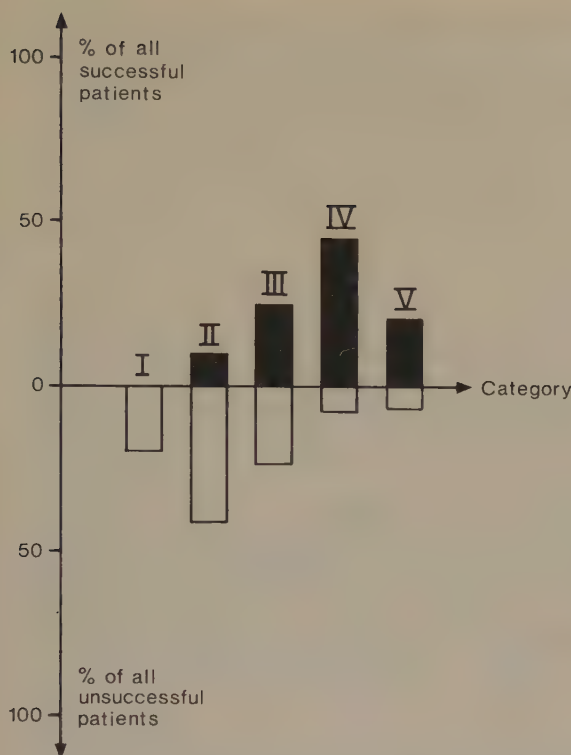


Fig. 1. Prognostic value of psychiatric categorization in TNS treatment. Black bars give percent of patients reporting satisfactory pain relief from TNS [3] during long term follow-up, white bars give percent of patients with no or insufficient pain relief from this treatment. Each patient was put into one of the following categories: I, mental illness; II, pathological personality; III, situational problems; IV, state of reactive mental decompensation; V, no psychopathological signs.

in the successful group. Furthermore it can be noted that 12 out of the 22 patients without RPC in the group with insufficient relief were judged to have pathological personality traits, whereas this was so in only 1 out of the 19 patients with an RPC in the group experiencing satisfactory relief.

Discussion

From the present findings it is evident that the psychiatric consultation has a predictive value for the outcome of TNS treatment in patients with chronic pain referred to a tertiary level pain unit (Fig. 1). However, the results have to be interpreted with some degree of caution since the study is retrospective in relation to the outcome of the TNS treatment even if this was not known to the psychiatrist.

In the group of patients not responding to TNS treatment there is an overrep-

resentation of mental illness and pathological personality traits (I–II). This indicates that such disturbances may contribute to or even constitute the cause of pain in the unsuccessful group [3,6,12]. Another important factor may be that these conditions create an unsuitable therapeutic environment for pursuing the TNS treatment. The incidence of reactive decompensation (IV) was higher in the successful group than in the unsuccessful group. A possible interpretation of this finding is that a state of decompensation is a normal reaction to the distress of pain caused by the physical lesion.

Whereas almost all patients with a successful outcome of the treatment had a relevant physical cause of pain (RPC), many patients did not benefit from the treatment in spite of the relevance of their physical disease to the perception of pain. It is probable that factors within categories I and II may interact with the RPC of the pain in several ways, so that TNS becomes an inadequate method of treatment. Thus, there may be an overlay of the psychiatric disorders upon the somatic symptoms, which makes the individual more sensitive to threatening experiences including pain [6]. Psychosomatic mechanisms or somatic symptom formation, i.e., the generation of pain as a mechanism of defense against anxiety or aggression caused by conflicts [cf., 14] may aggravate the pain in a vicious circle. Moreover, the RPC might be used by some patients to conveniently adhere to the sick role resulting in various social rewards ('abnormal illness behaviour') [8]. Among these patients a multidisciplinary approach to pain treatment is essential for a satisfactory therapeutic result [7].

Another interesting observation concerned the patients who had no RPC of the pain and failed to benefit from TNS treatment. Not less than 12 out of these 22 patients were found to have pathological personality traits and it can be supposed that these contribute to the development of the chronic pain condition. Most of the patients were evasive and affectively unstable with a repressive defense mechanism. In addition, some of them were rigid and stubborn, sometimes resembling cases with diffuse cerebral lesions. The patients in this sample then most frequently show signs that are generally described as hysterical traits [cf., 15]. The question of a possible relation between personality type, localization and type of painful symptom and response to therapy requires, however, studies with a more detailed approach.

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PERSONALITY FACTORS AS PREDICTORS OF SOCIAL ADJUSTMENT IN
CHRONIC PAIN CONDITIONS

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ABSTRACT

Ten patients with chronic pain of long duration were selected according to a clinical evaluation of their social adjustment to the pain situation. Five were well adjusted. The other five were not. All had pain with a similar, organic etiology and satisfactory symptomatic pain relief, achieved by transcutaneous nerve stimulation (TNS) or analgesic medication. The 'adaptive capacity' of each individual was independently assessed with psychological techniques and used as a predictor of social adjustment. The predictive value was good in individuals with high or low 'adaptive capacity'. Intermediate 'adaptive capacity' did not predict social adjustment and in this group, prediction might be improved by the addition of tests measuring factors such as motivation and rigidity. Identification of patients with good and poor 'adaptive capacity' might be helpful in understanding and aiding the process of adjustment to chronic pain.

INTRODUCTION

The variability of social adjustment in patients with chronic pain is a problem, highly relevant to the daily work at a pain clinic. Fordyce (7), Merskey (11), Sternbach (20), Pilowsky (14), and others, have suggested a variety of psychosocial factors, such as economic and affective reinforcement that can exaggerate or prolong both the experience and expression of pain.

In psychoanalysis, 'adaptation' is a central concept. "Generally speaking, we call a man well adapted if his productivity, his ability to enjoy life and his mental equilibrium are undisturbed" (9). Man has a certain psychological equipment to meet his average environmental situation, as well as more extreme ones.

Chronic pain is most certainly a factor hard to cope with, which may affect the productivity of the individual, his intrapsychic equilibrium and the ways in which he can enjoy life. For these reasons, social adjustment in chronic pain may well demand special adaptive resources, both within the individual and in his environment.

The aim of the present study was to investigate some psychological variables within the chronic pain patient, which might influence his adjustment to the condition. This was done in a selected group of well and poorly adjusted patients who had objective evidence of a relevant physical cause of the pain and were similar from a medical point of view. All experienced satisfactory symptomatic pain relief, in most cases from long-term treatment with transcutaneous nerve stimulation (TNS) (5, 6).

We postulated that the 'adaptive capacity' of the individual, could be measured and described by a group of psychological tests directed towards the study of various aspects of the personality, especially the ego concept as defined in dynamic psychology (9), viz.

- A/ Functioning of the so called "conflict free sphere of the ego" (9), i.e. cognitive functions such as thinking, memory, perception and verbal ability.
- B/ Ego functions involved in intrapsychic conflicts (between and/or within the id, ego and superego), i.e. personality aspects of adaptation to the environment. In ego-psychological terms this is for example defence mechanisms and cognitive style.

MATERIAL AND METHODS

Patient material

Ten chronic pain patients referred to the multidisciplinary pain unit at Lund University Hospital, were selected for the present study. The first three criteria for patient selection were: 1/ low back pain of more than five years duration with intermittent or permanent sciatic irradiation, and 2/ one or more surgical interventions including laminectomy, which meant that pain from postoperative scarring in most patients might have added to the original back problem, and 3/ pain relief $\geq 50\%$, (as measured by the patient on a visual analogue scale, 13) from symptomatic treatment, in most cases with TNS. The last criterion was one of 4/ adjustment to society. Five of the patients were selected as being well adjusted, e.g. because of their ability to continue working and to live a fairly 'normal' family and community life. The other five were selected because of their poor social adjustment. They were collecting sick benefits and had adopted new roles as 'disabled', with persistence of an inappropriate mode of acting in relation to their state of health, as judged by the physician. Care was taken that manual and intellectual workers were represented in both groups. Thus, the selection of patients reflected two distinctly different types of social adjustment in chronic pain conditions, which, from a somatic point of view, were similar.

The selection was made by the physician in our group and based on medical records and information obtained at multiple out-patient visits to the pain clinic. The interviews revealed that patients in both groups experienced themselves as often being ill, had to take special measures because of the pain such as frequent rest periods and were prevented by pain from doing things they would have liked to do. The patients clinically judged to be poorly adjusted often reported dissatisfaction with doctors and treatment. They also frequently stated that pain had influenced their sex life negatively. They did not regard themselves as able to work if the painful condition remained unchanged. - All in contrast to the well adjusted group.

The psychological testing was performed by one psychologist and the assessment of results by the other. The clinical classification as well as all records from previous treatments, were kept unknown to the psychologists.

There were six male patients in the group with a mean age of 48.5 (range 38-60) years, and four female patients with a mean age of 57.0 (range 43-74) years (Table 1).

Table 1. Demographic variables

<u>Patient number</u>	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10
Sex (female/male)	F	M	M	M	F	M	M	F	M	F
Age (years)	49	38	60	50	62	47	44	74	52	43

Psychometric techniques

The patients were asked to complete the following group of psychological tests:

A/ Cognitive tests

Koh's block design which measures visuo-spatial and logical-inductive capacity. The subject is asked to reproduce seven designs with coloured blocks. Each design has a time-limit, and credit is given for rapid performance (21).

Synonyms Reasoning Block (SRB):1 which measures verbal capacity. The subject is asked to choose one of five words as synonymous with a key-word (4).

Synonyms Reasoning Block (SRB):2 which measures logical-inductive capacity. Among groups of five geometrical designs presented four are alike in some way. The subject is instructed to identify the one that differs (4).

B/ Personality tests

The Arrow-Dot test ("IES") which is considered to give an estimate of the relative strength of the id (I), ego (E) and superego (S) of the subject. It is a perceptual motor task with 23 simple graphic problems. Each solution is scored as either an I, E or S response. The mean normal values are Id 3.1, Ego 17.8 and Superego 2.1 responses for the 23 possible responses (3).

The Colour Word Test (CWT) which measures strategies of adaptation to a conflict, expressed as the 'cognitive style' of the subject (18). The subject reads 100 coloured words, repeatedly 5 times. "Blue", "red", "green" and "yellow" are printed in, incongruent colours, e.g. is the word "blue" randomly printed in green, red or yellow. The time is scored after each 20th word. The score analysis reflects the adaptation to the stressful situation and is classified in the following four categories:

- S (stabilized), common pattern in normal subjects
- C (cumulative), common pattern in anxious subjects
- D (dissociative), common pattern in hysteric subjects
- CD (cumulative-dissociative), pattern seen in subjects with pronounced rigidity and in organic and depressive states.

The pattern of a particular subject - called "his cognitive style" - is a measure of how intrapsychic conditions such as anxiety, depression, dissociation and rigidity affect cognition.

The Defence Mechanism Test, (DMT), is a projective technique which describes personality within an ego-psychological frame of reference (10). Basically the assumption is made that an individual's personality is revealed through his mode of organizing perception, as described in 1971 by Smith and Kragh (19). Two pictures, each with an aggressive person attacking a neutral one, are shown in a tachistoscope. The exposure times are increased from 1/100 to 2 seconds in a series of 20 exposures. For each, the patient reports on what he sees. Distortions are scored and identified as signs of various defence mechanisms. The so called neurotic defence mechanisms (i.e. repression, isolation and reaction-formation) are regarded as more mature, whereas the so called primitive ones (i.e. projection, introjection and regression) in adults are signs of a disturbed personality.

Further information can be provided by a more detailed analysis of the CWT and DMT results. This was not used in our study due to the small sample size.

One group of cognitive tests and three personality tests were used. For each, a hypothesis was proposed regarding factors predicting good adjustment to chronic pain:

- 1/ Cognitive tests - a high general intellectual level,
- 2/ Colour Word Test - stable responding pattern (S-type).
- 3/ Arrow-Dot test - no marked intrapsychic conflicts, affecting the adaptation to an external stress situation such as the test. This would mean more ego-responses and less id-responses.
- 4/ Defence Mechanism test - no evident intrapsychic conflicts, which would mean less primitive and more neurotic defences.

RESULTS

1. Test group performance

In Table 2A the scores on tests of cognitive functions are presented. The calculated group mean of each intellectual performance test among the present patients was close to the mean of a normal population, as seen from Table 2B.

Table 2 A. Scores on cognitive tests (The Stanine scale, mean 5, S.D. $\pm$ 2)

Patient number	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10
Koh's block design	3	7	4	4	6	6	6	5	7	3
Synonyms Reasoning Block I	3	4	6	6	6	8	4	5	5	9
Synonyms Reasoning Block II	3	6	2	2	8	2	6	6	6	7
Mean	3.00	5.67	4.00	4.00	6.67	5.33	5.33	5.33	6.00	6.33

Table 2 B. Mean intellectual performance of the test group compared to a normal population

	Test group mean (Stanine)	Normal population mean (Stanine)
Koh's block design	5.1	5.0
Synonyms Reasoning Block I	5.6	5.0
Synonyms Reasoning Block II	4.8	5.0
All cognitive tests	5.17	5.0

The personality characteristics of the test group are seen in Table 3A and B. The frequency of primary response patterns on the CWT were five S (stable), three C (cumulative), one D (dissociative) and missing data from one (Table 3A). This distribution of cognitive styles is close to the one found in the normal reference sample. Also in the Arrow-Dot test (Table 3A) the group performance was close to what would be expected from a normal reference sample with a general predominance of ego-responses ($M_E = 16.2$, out of the 23 responses possible) (3).

Table 3 A. Classification of the Colour Word Test and scores on the Arrow Dot Test

Patient number	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10
Colour Word Test	C	C	D	C	S	S	S	-	S	S
Arrow-Dot Test										
Id-responses	11	11	11	1.5	9	0	6	6	4	1
Ego-responses	11	11	11	21.5	14	22	17	15	17.5	22
Superego-responses	1	1	1	0	0	1	0	2	1.5	0

Table 3 B. Frequency of DMT responses

Patient number	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10
'Neurotic' defence mechanisms										
Repression		5	-	4	-	2	-	2	4	15
Isolation		-	-	3	-	-	-	1	-	-
Reaction formation		-	1	-	-	1	-	-	-	1
'Primitive' defence mechanisms										
Introjection of opposite sex	-	-	20	1	2	13	2	6	-	16
Introjection of another object	-	-	-	-	-	-	-	-	-	13
Projection	-	2	-	-	-	-	-	-	-	-
Regression		1	-	-	1	-	-	-	-	-

Finally, the DMT results (Table 3B) in our sample were found to be similar to the standardization data of the test (17).

From the above, we concluded that our patients were a fairly representative sample of the population.

II. Assessment of individual 'adaptive capacity'

A/ Intellectual performance

From Table 2A is seen that patients 2, 5, 9, 10 and also 6, 7, 8 performed very well in the cognitive tests.

B/ Personality characteristics

The ego-psychological concept of adaptation to a conflict is well reflected by the CWT and the Arrow-Dot tests. Subsequently these two tests formed our main basis for analyzing the test performance with regard to 'adaptive capacity'. In the Colour Word test, it is seen from Table 3A, that patients 5, 6, 7, 9 and 10 represented S-types. These five patients adapted without doubt in the best way to the particular test situation.

In the Arrow-Dot test, two distinct groups emerged with three patients in each (Table 3A). Patients 1, 2 and 3, all had high id-scores indicating that they might be considered as 'impulse-ridden' with low 'adaptive capacity'. Patients 4, 6 and 10 had high ego-scores and appeared more "reflecting and reasoning" with good 'adaptive capacity' in the test situation. It also seemed reasonable to place patient 5 in the id-responding group and patient 9 in the ego-responding one. Patients 7 and 8 were difficult to classify.

In the DMT test, the most primitive mechanisms of defence, regression and projection were seen in patients 1, 2 and 4 (Table 3B). Introjection of the opposite sex was seen in a high frequency in patients 3, 6 and 10. Patient 10 as the only one also had introjection of another object and her structure of defences might be considered rather immature. From the results, in accordance with

hypothesis number four, it was concluded that patients 1, 2, 4, 6 and 10 had low 'adaptive capacity', because of the primitive quality of their ego-defence mechanisms.

III. Patient grouping according to 'adaptive capacity'

The well adjusted patients were known to be five and taking all test parameters together, patients 5, 6, 7, 9 and 10 appeared as having a better 'adaptive capacity' in stress conditions. Patient 9 fulfilled the requirements of all four hypotheses, patients 5, 6, 7 and 10 three out of four. Among the five patients considered to have a low 'adaptive capacity', patients 1 and 3 fulfilled no hypotheses, patients 2 and 4 one out of four and patient 8 two out of four. Looking at results from the three personality tests only, one patient (P9) fulfilled all three hypotheses related to these tests, three patients (P1, P2, P3) fulfilled none. The grouping of the patients did not change when results from cognitive tests were excluded.

IV. 'Adaptive capacity' related to social adjustment

As seen from Table 4, there was a total agreement between the physician's initial evaluation of social adjustment and the psychologists' evaluation of 'adaptive capacity' in patients 1, 2, 3, 6, 7 and 9.

Table 4. Relations between 'adaptive capacity' and social adjustment

		Social adjustment	
		Good	Poor
'Adaptive capacity'	High	P6,P7,P9	P5, P10
	Low	P4,P8	P1,P2,P3

Patients 5 and 10 were considered poorly adjusted in spite of a good 'adaptive capacity' while patients 4 and 8 appeared well adjusted, while showing only mediocre 'adaptive capacity' in the tests. In the four cases where there was disagreement, the patient history was of special interest.

Poor social adjustment/Good 'adaptive capacity'

Patient 5, a 62-year-old woman, had for six years been a regular out-patient at the Pain Unit. For many years, she was confined to a wheel-chair and did not take responsibility for herself, her family or her home. During the very last year she had started to show signs of improvement, being up on her feet for longer periods, taking an interest in her family, doing some household work etc.

Patient 10, an unmarried woman of 43 years, had not gone back to her previous intellectual work which was flexible and physically easy. Physical examination at the present time gave no reasonable explanation. She performed excellently in tests measuring verbal and logical capacity, as well as on the CWT and the Arrow-Dot tests. In the DMT, however, she showed signs of a personality deficiency with primitive defence mechanisms, such as introjection of objects and the opposite sex.

Good social adjustment/Poor 'adaptive capacity'

Patient 4 was a 50-year-old man, working full-time in a supervising job, having no marked problems in his family relations. He performed poorly in cognitive tests and had low scores on CWT and IES. An additional information from the CWT and DMT tests was his marked rigidity.

Patient 8 was a 70-year-old, poorly educated woman, who had functioned well for her entire life as a farmer's wife. She was in good spirits, but had difficulties in adjusting to the psychological test situation. Thus, she failed completely on the CWT and also revealed somewhat more id-tendencies on the Arrow-Dot-test. On the other hand she had a good score on cognitive tests and predominantly normal answers in the DMT.

DISCUSSION

We have used the concept of 'adjustment', as a social-psychological term which reflects the patient's relation to his environment, as observed through a general clinical evaluation. The concept of 'adaptive capacity' was used to describe the patient's internal resources to cope with his environment, as reflected in psychological test results. In our small and selected group of patients with chronic pain we attempted to control only one situational aspect, the organic cause of the pain, whereas other aspects were not looked into.

In the present study, we chose not to employ the commonly used questionnaire technique. This approach tends to yield the tested individual's conception of himself in relation to a particular person, the 'examiner'. Using the MMPI questionnaire (11), Cummings et al. (1) studied 74 patients, suffering from chronic pain, who attended a six week in-patient treatment program. The subjects were assessed before entering the program and after treatment. No significant differences between improved and unimproved were found in the MMPI variables. In another study, Pondaag and Oostdam (15) reported 48 lumbar disc patients undergoing psychological testing, before and six months after surgery. The group of questionnaires used discriminated the improved patients from the unimproved in 85 % of the cases. The highly disagreeing results between the two reports suggest that the questionnaire technique may be a less reliable measure and an unstable basis for prospective studies on the outcome of a treatment.

Agreement between 'adaptive capacity' and social adjustment was found in 6/10 patients (Table 4). When results from cognitive tests were excluded it was found that the single patient who fulfilled all three personality-related hypotheses for a high 'adaptive capacity' was socially well adjusted and the three patients who

fulfilled none of these hypotheses were all considered poorly adjusted to society (Fig.).

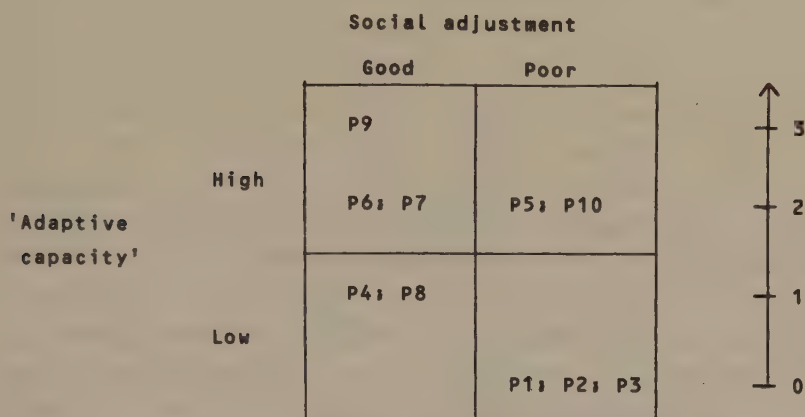


Figure. Relations between clinically assessed social adjustment and psychologically assessed 'adaptive capacity', considering the number of fulfilled personality-related hypotheses for each patient (arrow).

Among the other six patients, who fulfilled one or two personality-related hypotheses, both poorly and well adjusted individuals were found. Here other factors may have played an important role in determining what use the patient had made of his particular resources. The best possible use of an individual's 'adaptive capacity', considering the circumstances and the personality may not be identical from a psychological point of view and from society's point of view. A hysteric conversion syndrome for example such as a paralysis, sensory disturbance or pain condition, may from society's point of view represent a poor adjustment to a stressful situation, whereas from a psychological point of view this may be the best possible use of that individual's 'adaptive capacity'.

The disagreement between 'adaptive capacity' and social adjustment found in 4/10 patients might be interpreted as follows: Patient 5 had the psychological resources, but had not been able to make use of them until recently. She now appeared to be on her

way from poor to better adjustment, most likely as a result of the treatment by the Pain Unit. Patient 10 had likewise the necessary adaptive resources, but also had a personality deficiency, which she compensated for by symptom formation. This might have been one major component of her chronic pain syndrome.

The remaining two patients had low 'adaptive capacity' but were socially well adjusted. It seemed as if patient 4 had a resource for adjustment in his pronounced rigidity, an asset which prevented him from giving up earlier adopted patterns of behaviour, including going to work. This is in agreement with Hagberg's findings in another stress condition, viz. in a group of patients undergoing chronic hemodialysis, where pronounced rigidity correlated with good adjustment (8). Patient 8 was classified as having a poor adaptive capacity mostly because of her total failure with the CWT. Her poor education (not known in the test situation) and age, probably were largely responsible. Her other test results placed her just beneath the level considered to be good 'adaptive capacity'.

One of our hypotheses was that patients with high 'adaptive capacity' would perform better in cognitive tests than those with low 'adaptive capacity'. This was not found to be the case. Furthermore, the correlation between 'adaptive capacity' and social adjustment did not change when results from cognitive tests were excluded (Fig.). Thus, cognitive functioning did not seem to be a parameter related to social adjustment, although it might still be an important factor in how an individual will make use of his 'adaptive capacity' in a particular stressful situation.

We also hypothesized that the existence of intrapsychic conflicts, as measured by the three personality-related tests, would influence the social adjustment of the individual in chronic pain. Indeed, the ability to adapt to stressful situations, as measured by the Colour Word Test, was important and the Arrow-Dot test added

further information in this respect, differentiating 'impulse-ridden' patients governed by acute internal needs from those using reasoning and mature mechanisms for adaptation. From the qualitative analysis of the Defence Mechanism Test valuable information was obtained about the mechanisms of defence habitually used by each patient when dealing with anxiety. In our patient sample good social adjustment paralleled the use of more 'neurotic' mechanisms of defence, such as repression, isolation and reaction formation. This is in agreement with another study (8), in which patients adjusting well to hemodialysis were found to use predominantly 'neurotic' mechanisms of defence. It should also be noted that the primitive defence structures considered related to poor 'adaptive capacity' could be differentiated i.e. the regressive signs being the most malignant followed by projection and introjection.

It is interesting to note that all the patients selected for this study experienced satisfactory pain relief from symptomatic treatment, regardless of their degree of social adjustment. This is in agreement with results from an earlier study, where "situational problems" such as occupational or economical problems, loss of object or problems in personal relationships, among chronic pain patients with a relevant physical cause of the pain were found to be unrelated to the analgesic effect of treatment with transcutaneous nerve stimulation (12).

Being able to give a reliable prognosis of social adjustment in a patient with pain, threatening to become chronic, would be most valuable in clinical work. The results of the present study, albeit a small number of patients, suggest that one relevant parameter may be the 'adaptive capacity' of that individual, as specified in the three personality-related hypotheses. However, motivation and flexibility/rigidity might be other important factors, particularly in the group with intermediate 'adaptive capacity'.

The factors that indicate high 'adaptive capacity' are congruent with the standard requirements which indicate a patient suitable for short-term psychotherapy (16). Since the process of social adjustment in a chronic pain condition might be slow, patients with high 'adaptive capacity' might benefit from short term psychodynamic therapy in order to reduce the time necessary for rehabilitation, by making better use of their emotional resources. Patients having low 'adaptive capacity' because of factors which also make them less responsive to short-term psychotherapy, might still benefit from information and support.

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